DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, EDUCATION, AND RELATED AGENCIES APPROPRIATIONS FOR 1993

HEARINGS

BEFORE A

SUBCOMMITTEE OF THE

COMMITTEE ON APPROPRIATIONS
HOUSE OF REPRESENTATIVES

ONE HUNDRED SECOND CONGRESS

SECOND SESSION

SUBCOMMITTEE ON THE DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, EDUCATION, AND RELATED AGENCIES

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Printed for the use of the Committee on Appropriations

U.S. GOVERNMENT PRINTING OFFICE
55-258 WASHINGTON : 1992

For sale by the U.S. Government Printing Office
Superintendent of Documents, Congressional Sales Office, Washington, DC 20402

ISBN 0-16-038559-8

55-258 O—92——1

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NOTES:

The Honorable Silvio O. Conte was Ranking Minority Member of the Committee until his death on February 8, 1991.

The Honorable William H. Gray III resigned from the Committee on September 11, 1991.

DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, EDUCATION, AND RELATED PROGRAMS

MONDAY, MARCH 23, 1992.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

WITNESSES

DR. KENNETH OLDEN, DIRECTOR, NIEHS
DR. BERNADINE P. HEALY, DIRECTOR, NIH
CHARLES E. LEASURE, JR., ASSOCIATE DIRECTOR FOR MANAGEMENT
ROBERT C. PATRICK, BUDGET OFFICER, NIEHS
DENNIS P. WILLIAMS, DEPUTY ASSISTANT SECRETARY, BUDGET, DHHS

INTRODUCTION OF WITNESSES

Mr. NATCHER. At this time we take up the budget request for the National Institute of Environmental Health Sciences. We have before the Committee Dr. Kenneth Olden.

Dr. Olden, before you give us your statement, tell us who you have with you there at the table.

Dr. OLDEN. Thank you, Mr. Chairman.

To my right, I have Mr. Dennis Williams from the Department and, of course, Dr. Bernadine Healy, Director of NIH; to my left is Mr. Charles Leasure, Associate Director for Management, and Mr. Robert Patrick, Budget Officer for NIEHS.

Mr. NATCHER. Thank you.

Dr. Olden, we will be pleased to hear from you.

OPENING STATEMENT

Dr. OLDEN. Mr. Chairman and Members of the Committee, I am pleased to defend the President's budget request for the National Institute of Environmental Health Sciences. The Institute has made significant progress. With your permission, I would like to submit my statement for the record and spend a few minutes talking about the new directions for the Institute.

The National Institute of Environmental Health Sciences has a very important role to play both in improvement of public health and in containment of the health costs of the Nation. Human health is determined by both genetic and environmental factors—or by the interplay between the two over the course of a lifetime. Understanding these influences and the nature of their interaction is of critical importance in elucidation of the role of the environment in the etiology or progression of human diseases and dysfunctions.

ROLE OF THE ENVIRONMENT IN HUMAN HEALTH

For a variety of practical or historic reasons, environmental health research has been heavily directed toward the identification of physical and chemical factors that cause cancer. This research has been critical to the national cancer program and must be continued. However, the research programs of NIEHS must place greater emphasis on other human diseases; otherwise, the health of the American people is not being adequately protected.

The study of how environmental factors affect human health is at a promising juncture. In the past, techniques for studying environmentally-caused disorders were crude and generally lacked the sensitivity and specificity to detect subtle alterations or changes in disease states. Now, with the advent of sophisticated new tools—tools such as polymerase chain reaction techniques, improved gene cloning techniques, and molecular modeling—we are poised to initiate research that will develop a fundamental understanding of the role of the environment in the etiology of human diseases.

Historically, environmental health science research has been divorced from prevention in health research. Progress in basic environmental health science research has evolved to the point where this new knowledge can be applied to treat human diseases. Such studies in humans are important in that they will reduce the necessity to extrapolate studies to humans and will provide a basis for establishing human standards for exposure. Also, animal models for many human diseases do not exist. To reverse the historical trends in environmental health science research, the Institute is in the process of reshaping old programs and creating new ones to emphasize the more global mission of the Institute with respect to human diseases.

PRIORITY PROGRAMS

During the next five years, the Institute will place highest priority on initiating or strengthening the following programs:

First, the Institute will emphasize mechanisms by which chemical and physical agents in the environment cause human diseases. Our objective is to strengthen our ability to predict toxic effects on humans of physical, chemical, and biological agents. Progress in understanding the environmental basis of disease depends on both the identification of causative agents and the elucidation of their mechanisms of action.

Knowledge of mechanisms is especially important in those cases where elimination of exposure will take years to achieve and where rational design of prevention is desired.

Second, the Institute will strengthen its research programs that target non-cancer endpoints. These studies will include birth defects, infant mortality, infertility, bronchial asthma, Parkinson's and Alzheimer's diseases.

Third, we will seek the development of biomarkers of exposure, effect, and susceptibility. Biomarkers represent tools for early identification of exposure to environmental toxins before the onset of disease. Epidemiologists estimate exposure based on average for the general population. This process is obviously less precise in estimating health outcomes than using scientific markers of individual exposure. Individuals at risk can be counseled to change their behavior.

Fourth, the development of clinical and prevention research programs to complement ongoing basic research. The first clinical studies will focus on: The role of environmental chemicals with estrogen-like activity on the onset of precocious puberty; and the development of better chelation and nutritional intervention therapy for the management of lead poisoning. An ad hoc advisory group recently recommended the development of a third clinical study to examine the environmental component of bronchial asthma.

Five, is prevention research. Lead poisoning research has been identified as the initial effort in this area, as this may be the most devastating environmental disease in children. The objective for the research program will be to devise strategies for prevention through education and counseling of high-risk groups, such as pregnant women, parents of young children, and the inner-city poor.

Finally, environmental equity. The objective of these studies will be to determine the extent to which preventable environmental factors contribute to inequities in disease occurrence that exist between various ethnic groups.

Mr. Chairman, the President's 1993 budget request for NIEHS is $261,513,000. I will be pleased to respond to any questions you might have.

[The statement of Dr. Olden follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement of the Director
National Institute of Environmental Health Sciences

The National Institute of Environmental Health Sciences (NIEHS) has a very important role to play both in improvement of the public health and in containment of the health cost of the Nation. Unlike the other institutes of the National Institutes of Health--that focus on specific diseases--NIEHS supports research on the etiology of most human diseases because of their environmental association. Thus, the potential contribution of NIEHS to the broad mission of the NIH is unparalleled within the biomedical research enterprise of the Federal Government.

Human health is determined by both genetic and environmental factors, or by the interplay between the two over the course of a lifetime. Understanding these influences and the nature of their interaction is of critical importance in elucidation of the role of the environment in the etiology or progression of human diseases or dysfunctions. We need to give higher priority to establishing the role environmental agents play in human health. This understanding is particularly critical when you consider that the causes of most chronic diseases, including birth defects and most degenerative neurological disorders, are unknown.

Environmental health science research is be broadly defined to include studies of the causes, prevention, and treatments of the entire array of non-genetic factors that contribute to human disease and dysfunction, but for a variety of practical and historical reasons, environmental health science research has been heavily directed toward the identification and characterization of physical and chemical factors that cause cancer. Information from this research has been translated into regulatory policies intended to reduce or eliminate community and occupational exposures to substances presenting health hazards. For example, approximately one-third of our current appropriation goes to support cancer-related research. This research has been critical to the national cancer program. Although toxicological testing, with a focus on cancer is important, attention must also be given to other human illnesses or dysfunctions. The research programs of NIEHS must place greater emphasis on other human diseases; and in doing so, the health of the American people can be adequately protected.

Since becoming Director of the NIEHS, we have begun to reshape old programs and create new ones to emphasize the more global mission of the Institute with respect to human diseases. For example, greater emphasis will be placed on studies to examine the effect of the environment on reproductive health, neuroendocrine disorders, immune disorders, aging, and kidney diseases.

To prevent human illness, we must determine the role of both genes and the environment in the disease process. Rapid progress is being made in mapping the human genome and establishing a causal relationship between genes and specific diseases, but advances in our knowledge of how environmental agents affect human health has been less spectacular. New and expanded research into environmental influences on human health should be carried out if we are to understand the full range of biological processes and disease states of clinical importance.

In the absence of evidence to the contrary, it is reasonable to assume that the environment may play a major role in the etiology and/or progression of most human diseases or dysfunctions. In the past, methods were not sufficiently specific to establish causal relationships or they were not sensitive enough to detect subtle or subclinical effects. Also, people are exposed to multiple environmental agents simultaneously and at widely varying doses, complicating the ability to single out the role that a single environmental agent might play in a particular disease. Additionally, there is often a lag time of several years between a critical environmental exposure and manifestation of the resulting disease. Finally, differences in individual and population susceptibility has confounded interpretation. However, with recent advances in research methodology in molecular and cellular biology, NIEHS is now prepared to make rapid advancements in our understanding of the role of the environment in the initiation or progression of various diseases. For example, we can now detect or amplify subtle molecular or biochemical changes that take place in the cell in response to an environmental insult and the biochemical basis for differences in individual susceptibility can now be studied.

Another possible reason for the slow progress in environmental health science research is that there has been too little emphasis on studies to elucidate mechanisms by which environmental agents cause diseases. Even in the case of carcinogenesis, studies too often have not progressed beyond hazard identification. Without knowledge of mechanisms, a rational basis for design of secondary prevention/intervention strategies cannot be developed. Attention to mechanisms of action is especially crucial in those cases where elimination of exposure will take years to achieve. This mechanistic research is one of the high priorities for this Institute.

Another area that requires enhancement is research to develop biomarkers of exposure, effect and susceptibility. These markers are needed for epidemiological studies to establish an association between disease patterns and environmental risk. Many of the limitations encountered by environmental epidemiologists could be overcome if sensitive, reliable, and convenient biomarkers were developed to ascertain if an individual or population has been exposed and, ideally, to quantify that exposure. Presently, epidemiologists are able to detect only the more obvious outcomes of environmental exposures and can relate these results only to the general population rather than to individuals by reconstruction of past exposures. Since all individuals or populations are not equally susceptible to exposure to a given environmental toxin, knowledge of the biochemical or molecular basis for such differences would be useful in the development of practical prevention/ intervention strategies targeted to the appropriate individuals or populations.

Historically, environmental health science research has been divorced from prevention and clinical research even though technology transfer takes place most rapidly in an arena where basic, applied, prevention and clinical research exist together. Recent progress in basic environmental health science research has evolved to the point where this knowledge can be applied to prevent or treat human diseases. Such studies in humans are important in that they will reduce the necessity to extrapolate from laboratory model systems to human exposure and will provide a more scientific basis for establishing human standards for exposure.

The NIEHS has embarked on a new effort to develop intramural clinical research to complement ongoing basic research. Prior to this year, our efforts in human studies were confined mainly to epidemiology.

The three criteria used to decide which clinical programs are ready for development are: (1) the health problem under investigation should have an environmental association, (2) a cutting-edge effort in basic research on the topic should be ongoing at the NIEHS, and (3) a comparably first-rate clinical unit should exist at one of our local medical centers.

Our first clinical effort took advantage of a research opportunity to study the basis for the environmental perturbation of the advent of puberty in children. We have identified a cohort of boys and girls who are entering puberty as young as three to four years of age. This disorder, known as precocious puberty, occurs in one child in to ten thousand. In addition to onset of sexual maturation, the growth of the affected children is stunted and they acquire the physical appearance of adults. The objective of the clinical trial is to investigate the hypothesis that hormone-like chemical agents in the environment are responsible for this disorder. Though this disorder is not life threatening, it exacts a physical and psychological toll on youngsters.

During 1992, we will complete protocols for clinical trials in pulmonary medicine, focusing on bronchial asthma; and another in childhood lead toxicity focusing on chelation and nutritional therapy. Both diseases affect millions of Americans and are clearly caused by environmental exposures.

These clinical studies provide the opportunity for the Institute to extrapolate findings from animal studies to the practice of medicine.

Lead is an environmental toxin that continues to be a serious threat to the health of the developing fetus, children, and adults in the United States. Exposures resulting from the ingestion of lead-contaminated paint chips, dust, and water can cause neurological, developmental, and behavioral disorders. For example, mothers ex- posed to lead have higher frequency of spontaneous abortion, low birth weight babies and babies of younger gestational age. Human exposure to lead has been dramatically reduced in recent years following the removal of lead from gasoline and paint; however, there are still four million American children with elevated levels of lead.

Accumulation of lead in the bone is an especially serious problem for pregnant women who mobilize lead, along with calcium, to provide calcium for the developing fetus and during osteoporosis, respectively. In fact, the progressive loss of memory and degeneration of brain function in the elderly may, at least in part, be related to mobilization of bone lead.

There is now a growing body of evidence that there may be no safe level for human exposure to lead. Children, because their brains are still developing, are particularly vulnerable to adverse effects of lead. Additionally, although lead poisoning can occur in all socioeconomic groups, the urban poor seem to be the primary victims. Until 1991, blood-lead levels of 25 ug/dL had been thought safe. However, it has recently been shown that levels as low as 7-10 ug/dL are associated with decreased intelligence and slower neurobehavioral development. Although the effects are subtle, they translate into a significantly higher likelihood of learning disabilities and school drop-out later in life.

At the same time that the Institute was supporting the above applied research program, basic research into the understanding of lead toxicity was also being conducted. These studies showed that lead affects metabolism of several important nutrients, particularly Vitamin D, calcium, and iron, and that nutrition affects lead absorption in the gastrointestinal tract. These findings suggest that nutritional factors might ameliorate the subtle neurobehavioral defects associated with low-lead exposures. This possibility was further substantiated by epidemiological studies showing that poor nutritional status exacerbates the effect of lead in children.

The diagnosis of body lead relies heavily on determination of the concentration of lead in the blood. The problem with measuring blood lead is that it represents a "snap-shot" of recent exposures, but provides no indication of the total body burden. Therefore, additional studies are needed to develop X-ray fluorescent or other techniques for measurement of bone lead.

Another area requiring additional studies is the development of better lead chelating agents. Chelators, such as calcium-EDTA, form complexes with lead and increase its rate of excretion in the urine. Calcium-EDTA has been used for chelation therapy for the past 35 years; however, it has several shortcomings. First, it cannot distinguish between lead and other metals in stimulating urinary diuresis; many of these metals are essential for normal body function. Second, the administration of calcium-EDTA to chelate blood lead has such serious side effects that the patient has to be hospitalized for 4 to 5 days. Third, calcium-EDTA therapy does not remove lead stored in the brain. Thus, additional studies are needed to test or develop new chelating agents that do not have those shortcomings.

Thus, a coordinated effort, including both applied and basic research into the mechanism of lead toxicity, has brought us to the point where we can now design and test potential intervention strategies using both behavioral and clinical approaches. Research efforts of this nature will continue to be needed to address the valid concerns the American people have about other environmental causes of diseases.

Mr. Chairman, the budget request for the National Institute of Environmental Health Sciences is $261,513,000. I would be pleased to answer your questions.

OLDEN, DR. KENNETH

Director, National Institute of Environmental Health (NIEHS) and
Director, National Toxicology Program (NTP)

July 22, 1938. Parrottsville, Tennessee

Education: B.S., Knoxville College, 1960; M.S., University of Michigan, 1964; Ph.D., Temple University, 1970 (research done in absentia at the University of Rochester).

Professional History: 1964-65, Research Assistant, Department of Biological Chemistry, Columbia University. 1970-74, Research Fellow and Instructor of Physiology, Harvard University Medical School. 1974-77, Senior Staff Fellow, Division of Cancer Biology and Diagnosis, National Cancer Institute. 1977-78, Expert (Biochemistry) Division of Cancer Biology and Diagnosis, National Cancer Institute. 1978-79, Research Biologist, Division of Cancer Biology and Diagnosis, National Cancer Institute. 1979-82, Associate Director for Research, Howard University Cancer Center, and Associate Professor of Oncology, Howard University Medical School. 1982-84, Associate Director for Research and Deputy Director, Howard University Cancer Center, and Associate Professor of Oncology, Howard University Medical School. 1984-85, Associate Director for Basic Research and Deputy Director, Howard University Cancer Center, and Professor of Oncology, Howard University Medical School. 1985-91, Director of the Howard University Cancer Center and Professor and Chairman of the Department of Oncology, Howard University Medical School. 1991-present, Director, NIEHS and NTP.

Professional Organizations: American Society for Cell Biology; American Society of Biological Chemistry; American Association of Cancer Research; Society for Biological Response Modifiers.

Honors, Awards: Porter Development Postdoctoral Fellow, 1970. NIH Postdoctoral Fellow, 1970-73. Macy Faculty Fellow, 1973-74. Citation Classic, Current Contents, Life Sciences, 1980. Member, Division of Cancer Biology and Diagnosis Board of Scientific Counselors, National Cancer Institute, 1981-1985. Member, Public Policy Committee of the American Society for Cell Biology, 1984. Co-Chairman, Mid-Atlantic Region of National Black Leadership Initiative on Cancer, 1987-89. Member, Board of Directors, Association of American Cancer Institutes, 1987-90. Member, Division of Cancer Treatment Board of Scientific Counselors, National Cancer Institute, NIH, since 1988. Selected as "One of sixteen historical and contemporary role models" for the Museum of Science and Industry, Chicago, IL, 1988. Member, Board of Directors of Association of Minority Health Professions Schools, 1988-present. Member and Co-Chairman of National Advisory Committee on Socio-Economically Disadvantaged of The American Cancer Society, 1988. Member, Advisory Panel Council for Cell Biology, National Science Foundation, 1989-90. Presidential appointment to membership on the National Cancer Advisory Board, 1991. Associate Editor of Cancer Research, The Journal of the National Cancer Institute, and Cell Regulation.

Mr. NATCHER. Thank you, Dr. Olden.

Now, Doctor, how long have you been in your new assignment as Director of the Institute?

Dr. OLDEN. I have been there since June 26, 1991.

Mr. NATCHER. How long did your predecessor, Dr. Rall, serve as Director?

Dr. OLDEN. I believe he served just short of 20 years.

CHALLENGES IN ENVIRONMENTAL HEALTH SCIENCES

Mr. NATCHER. As you take over, what do you see as the major problems facing the field of environmental health generally and the Institute in particular at this time, Dr. Olden?

Dr. OLDEN. Well, I think the major challenge is to integrate cell and molecular biology, toxicology, and mathematical modeling into a science to strengthen the way we do risk assessment.

OZONE DEPLETION AND GLOBAL WARMING

Mr. NATCHER. What can you tell the Committee about your own view on the seriousness of the ozone depletion and global warming issues, about which people are very much concerned, Dr. Olden?

Dr. OLDEN. Well, certainly global warming and ozone depletion are very high priority items on the research agenda of the Institute. We have been working with the Environmental Protection Agency to address the ozone issues. Technically, we are interested in mechanism; we are interested in defining biomarkers for ozone; and we are interested in the synergism between ozone and other environmental pollutants.

ENVIRONMENTAL EQUITY

Mr. NATCHER. What do you mean by the term "environmental equity" which appears in the budget documents for the first time this year? What do you mean, Dr. Olden?

Dr. OLDEN. Well, it certainly has been established by the Environmental Protection Agency and other groups that the contribution of certain chemical industries, hazardous waste sites, incinerators, smelters, et cetera, are distributed in communities where mainly the socioeconomically disadvantaged live. It has been asserted that the diseases and the incidence of diseases in these communities may be associated with the presence of those industries due to the air pollution. Whether that is true or not needs to be established, I think, from a scientific point of view.

TASK FORCE IV

Mr. NATCHER. The budget documents describe a special advisory group called Task Force IV to review future direction for the Institute. I believe recommendations were due in February. Tell us, if you will, has this process been concluded and has the report been issued?

Dr. OLDEN. Yes, Mr. Chairman. The report has been completed, and we have submitted the report to Congress.

Mr. NATCHER. Are you generally satisfied with the task force thus far, or do you believe additional work needs to be done by the Institute on these issues?

Dr. Olden. I am very pleased with the report, Mr. Chairman. It is an excellent report. It is succinct, to the point, and I think it identifies the issues I pointed out in my opening statement as major issues that we could address.

Mr. Natcher. Dr. Olden, if you will, at this point in the record place an executive summary of the report. Place that in the record for us.

[The information follows:]

REPORT OF TASK FORCE IV

HUMAN HEALTH AND THE ENVIRONMENT: SOME RESEARCH NEEDS

Executive Summary

Clerk's Note: The full text of this Summary is available in the Committee files.

CANCER-RELATED RESEARCH

Mr. NATCHER. In your written statement you seem to indicate that too large a portion of the Institute's resources have been devoted to cancer. Will the 1993 budget make any significant changes in the proportion of your funding which is targeted at the cancer problem? Are there any major changes?

Dr. OLDEN. Mr. Chairman, I cannot say that there will be major changes, but what I hope to do is take a look at how we are managing our resources internally and divert as much of the resources as possible to the areas that I mentioned in my opening remarks.

However, in a time of budget crisis for the country—of financial constraints, I will have limitations. What I anticipate doing is, as the budget of the Institute grows over the years, to put most of those resources into other disease end points.

However, I want to emphasize I will not decrease the amount of dollars currently spent for cancer-related research. We are going to develop some programs with Dr. Broder of the NCI to deal with the impact—possible impact—of the environment on cancer. We have discussed that. It will take new resources.

NEW FACILITIES

Mr. NATCHER. Last fall Congress began funding to begin construction of new facilities in the main campus in North Carolina. What is the current status of this work?

Dr. OLDEN. We have the blueprints all finished. It is out for bidding for construction. We ended up getting $7,800,000 through the appropriation process. Dr. Healy gave us $2,200,000. So we have $10,000,000. That project is essentially ready to go forward as soon as the bids are returned.

Mr. NATCHER. The Committee has seen cost estimates for this project over the years ranging from $45,000,000 to $55,000,000. What is your current estimate of the total cost of this construction to complete? Give us a good figure.

Dr. OLDEN. The figure that we have is $62,000,000. With the $10,000,000 that we have, we hope to prepare the site and put up the shell. That will go forward in a matter of weeks.

Mr. NATCHER. Do you think this is a sound figure?

Dr. OLDEN. Yes. That is our best estimate.

Mr. NATCHER. Mr. Obey, I yield to you.

Mr. OBEY. Doctor, let me just follow up on that question.

What will the Institute need next in order to move forward on that building?

Dr. OLDEN. Well, Mr. Obey, we need about $52,000,000 in order to complete the project. We can take any portion of that any time it is appropriated.

NATIONAL TOXICOLOGY PROGRAM

Mr. OBEY. Let me ask you about the toxicology program about which you and I have talked before.

Dr. OLDEN. Right.

Mr. OBEY. Eight years ago, the National Academy of Sciences issued a report in which it found a majority of heavily-used compounds had not been tested. Do you recall what percentage had not?

Dr. **Olden**. It was 20 to 25 percent of the chemicals in the marketplace that had not been adequately tested.

Mr. **Obey**. What other Federal agencies test chemicals for chronic and long-term toxicity?

Dr. **Olden**. NIOSH and the National Center for Toxicological Research, I think, are the only two.

Mr. **Obey**. What percentage of the research do you think is done by you?

Dr. **Olden**. I would say 94 percent is done by us; 5 to 6 percent is done by NIOSH. About 0.2 percent is done by the National Center for Toxicological Research.

RESEARCH CONTRACTS

Mr. **Obey**. What was the money you submitted for the R&D contract line? What did you present to Dr. Healy in your request?

Dr. **Olden**. It was $88,000,000.

Mr. **Obey**. How much was the request to OMB?

Dr. **Olden**. $66,000,000.

Mr. **Obey**. And you got?

Dr. **Olden**. $60,000,000.

Mr. **Obey**. Would you provide for the record a chart depicting the National Toxicology Program's carcinogenicity study since 1981 and include the funding for the National Toxicology Program during that time period?

Also, at that point include for the record information about what has happened to the average cost for studying the chemical over the past decade.

Could you also provide for the record the funding in dollars, the FTEs, in the area of intramural research, epidemiology and risk assessment and toxic research and testing over the past 10 years?

[The information follows:]

National Toxicology Program

Number of NIEHS-Funded Carcinogenicity Study Starts

Fiscal year:	
1981	54
1982	43
1983	15
1984	8
1985	18
1986	7
1987	6
1988	8
1989	8
1990	10
1991	8
1992	8

Total NTP Funding

Fiscal year:	
1981	$70,522,000
1982	72,921,000
1983	71,890,000
1984	77,265,000
1985	78,153,000

1986	76,984,000
1987	78,738,000
1988	80,522,000
1989	83,976,000
1990	82,076,000
1991	81,130,000
1992	81,855,000

NATIONAL TOXICOLOGY PROGRAM—AVERAGE COST PER STUDY (SUBCHRONIC AND CARCINOGENICITY)

[In thousands of dollars]

Route of exposure	Fiscal year—	
	1982	1992
Dosed feed	800	2,665
Inhalation	1,610	5,080

National Institute of Environmental Health Sciences

INTRAMURAL RESEARCH

Intramural Research consists of three research divisions, the Division of Intramural Research, the Division of Biometry and Risk Assessment, and the Division of Toxicology Research and Testing, along with several support staff. Funding for the Intramural Research program during the last 10 years has been as follows:

Fiscal year	Amount	FTE
1983	$46,516,000	594
1984	47,727,000	608
1985	54,077,000	587
1986	51,906,000	588
1987	57,789,000	603
1988	59,446,000	605
1989	62,157,000	581
1990	64,809,000	583
1991	67,922,000	615
1992	69,744,000	624

Dr. OLDEN. The budget for NTP contracts has been relatively constant over the past 12 years at around $52,000,000. That is in actual dollars. If we look at that in constant dollars, it goes from $52,000,000 down to about $28,000,000.

NIEHS GROWTH VS. OTHER INSTITUTES

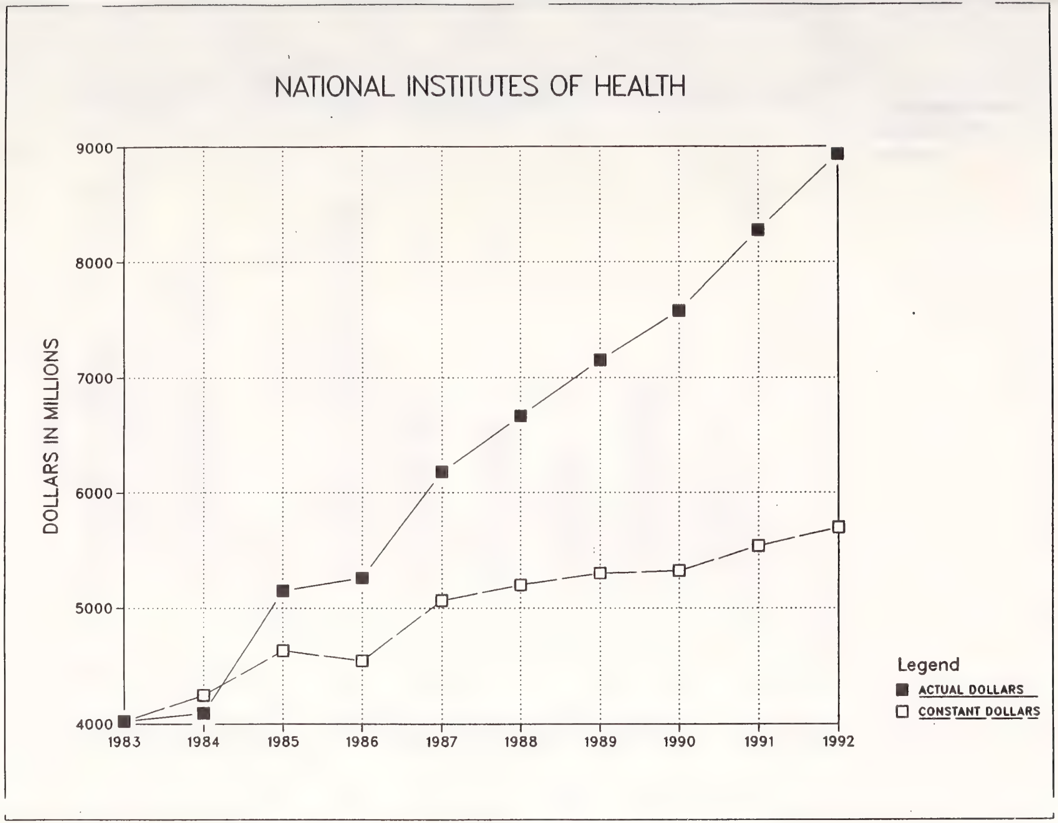
Mr. OBEY. My concern—and I am curious to see whether your charts coincide with mine—is if you take a look at NIH budget and look at the actual dollars it looks good, but when you look at the constant dollars, it looks—not bad, but nothing to write home about, either.

Then if you take a look at what has happened at NIH each year going back to 1984 and compare that in each and every year with what has happened with your Institute, your Institute seems to be the last dog in the parade as I look at what has happened. It is being allocated much less than an average share.

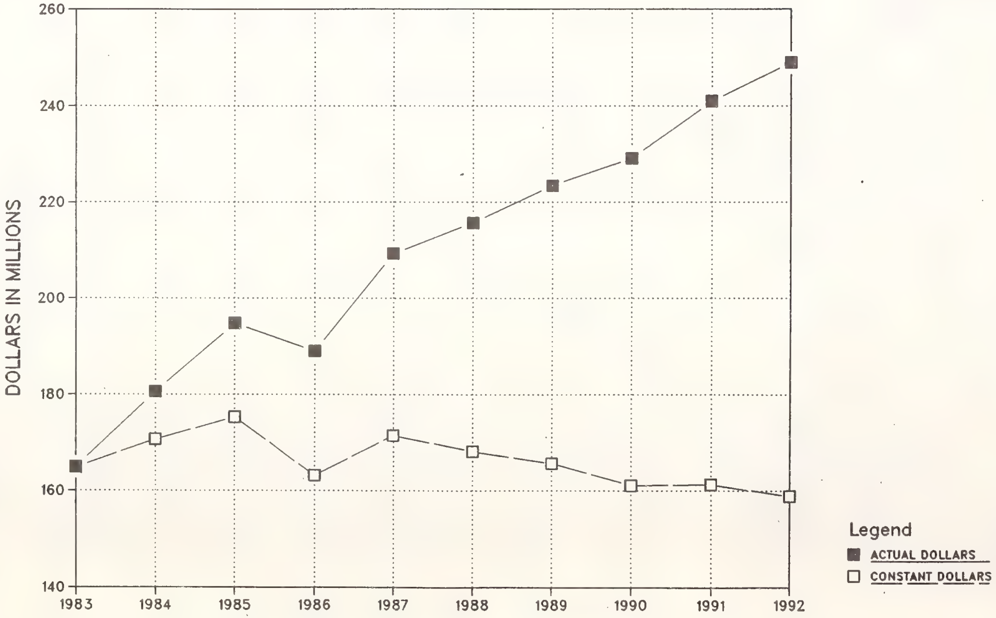
What bothers me, as I understand it, is that if you take a look again at NIEHS, if you take a look at the current dollars versus constant dollars, you have been on a small decline in constant dollars since 1983, which is not the case with most other institutes.

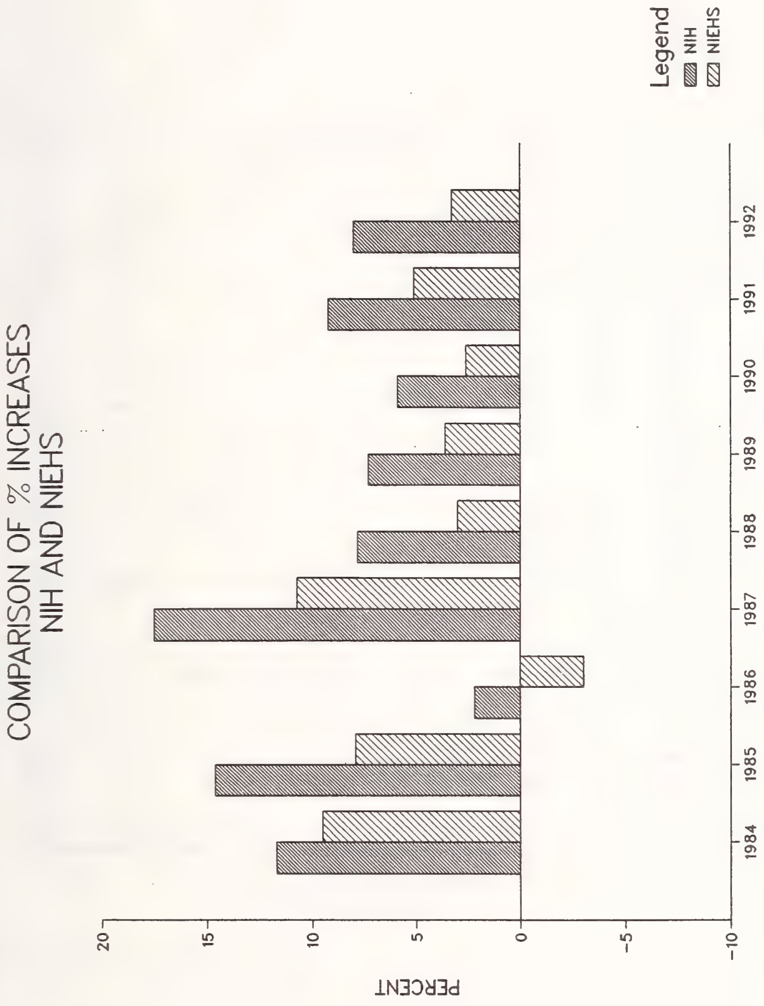
Then take a look at what has happened to the environmental health centers—I will put these charts in the record—you see a picture that looks pretty comfortable in terms of normal dollars but constant dollars present a very different picture again—a significant decline.

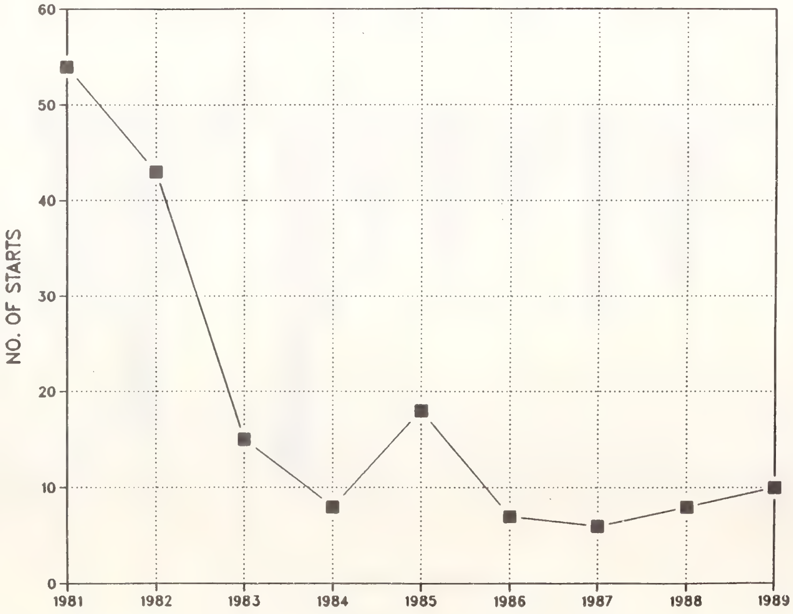
[The information follows:]


NATIONAL INSTITUTES OF HEALTH
DOLLARS IN MILLIONS
9000
8000
7000
6000
5000
4000
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
Legend
■ ACTUAL DOLLARS
□ CONSTANT DOLLARS

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

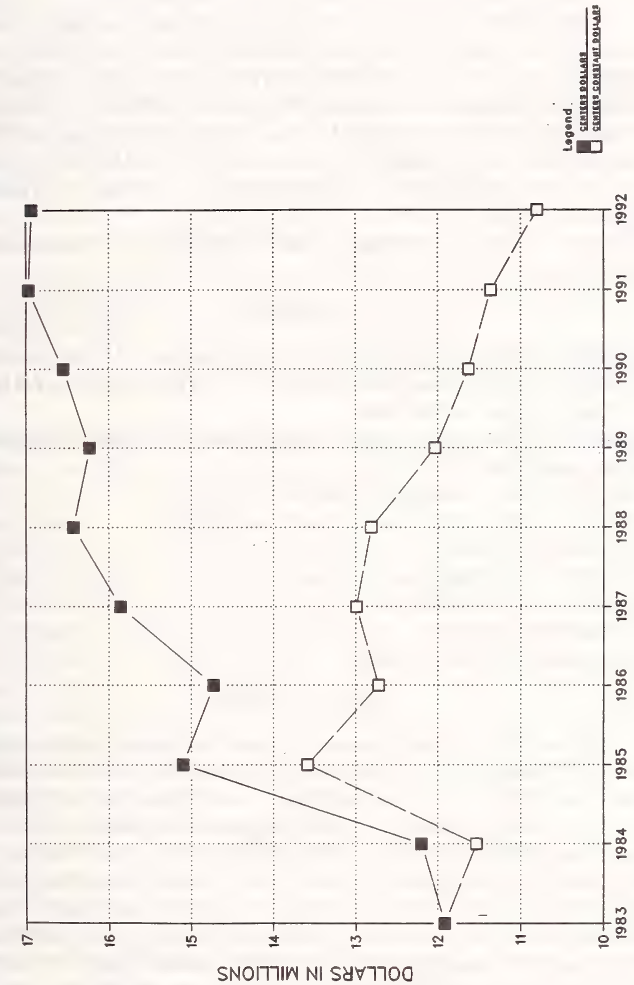



COMPARISON OF % INCREASES
NIH AND NIEHS
PERCENT
20
15
10
5
0
-5
-10
1984
1985
1986
1987
1988
1989
1990
1991
1992
Legend
NIH
NIEHS



NIEHS/NTP FUNDED CARCINOGENICITY STUDY STARTS

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
RESEARCH CENTERS



Mr. **Obey**. Then if you take a look at your study starts for the National Toxicology Program, that sure as the devil doesn't look like a trend that would impress anybody over the last decade.

So I think you are being shortchanged, Doctor. You provide the only training in government that I am aware of for environmental and occupational and health personnel. We still have—my assumption is that we still have an inadequate number of highly-trained toxicologists, correct?

Dr. **Olden**. That is correct. That was the recommendation of the task force report.

TRAINING

Mr. **Obey**. There is a tremendous need at all levels for toxicologists. Last year we had $10,900,000 for training at NIEHS, right?

Dr. **Olden**. That is correct.

Mr. **Obey**. What was your budget request this year to NIH for that same purpose?

Dr. **Olden**. We requested $14,200,000.

Mr. **Obey**. What was the request to OMB?

Dr. **Olden**. $11,300,000.

Mr. **Obey**. The President gave you?

Dr. **Olden**. About $10,900,000.

Mr. **Obey**. All right.

Thank you, Mr. Chairman.

LEAD EXPOSURE

Mr. **Stokes**. Dr. Olden, reading your formal statement, you make a statement that lead is an environmental toxin that continues to be a serious threat to the health of the developing fetus, children and adults in the United States. Exposure resulting from the ingestion of lead-contaminated paint chips, dust and water can cause neurological, developmental and behavioral disorders. This is an area in which I have had a great deal of concern, and we have had discussion with your Institute over a number of years about this problem. Are we making any progress at all? Are we learning any more about lead toxicity and its effect on children and adults, et cetera?

Dr. **Olden**. The answer is yes. We are making remarkable progress, in fact. Certainly on the basic science side. Recent studies have demonstrated that moderate to low level leads certainly are not safe, and they do lead to development and neurological abnormalities.

We are also making some progress on the clinical side. Some chelators, agents that will reduce lead levels in the blood, have been introduced to the marketplace. What we propose to do in our clinical trials is compare the newer ones with the ones that have been in existence. I think we can improve on the chelators and the ones on the marketplace need to be tested in humans.

One area where there has not been a lot done, and we propose to do it, is in the area of prevention. That is an area that will pay dividends in the short term. I think research should be initiated in that area.

Mr. STOKES. I agree with you. What are you proposing to do in that area in terms of prevention and education?

Dr. OLDEN. We have some ideas, but, basically, we will not do this as an intramural effort. We will do it as a grant mechanism. We will put out an RFA inviting people in the field to come in with their best ideas as to how one might be able to reduce lead. I can say we have done some preliminary studies, and we have demonstrated that certainly you can go into homes and educate families to do some very simple things: put contact paper on a window sill, mop the floor frequently, put contact paper over walls that contain lead-based paint, encourage their children not to eat the lead. I think clearly we can get improvement in blood lead levels. You can clearly measure the lead in the blood.

That is the kind of thing we are looking for, although I don't want to say that that is exactly what the prevention program will look like.

Mr. STOKES. In terms of lead paint poisoning and the whole lead paint problem, is this a program that is relegated particularly to the inner city or do we find this to be a problem in the suburban environment also?

Dr. OLDEN. It is a problem nationwide both in inner cities and suburbia. The problem is exaggerated in the inner city because the lead in the soil is higher in the inner city than it is in suburbia because of the cars that come in and out that use lead-based gasoline.

Also, because of the socioeconomics—these people certainly have other health problems. They are not as educated and certainly the dwellings are older and there is more chipping paint and probably the plumbing is not as good as the plumbing is in the suburbs. And access to health care is another issue.

So I would say certainly we are not immune to it in suburbia, but the problem is exacerbated in the city areas.

Mr. STOKES. Do you have funds to begin the clinical trials with respect to lead and children?

Dr. OLDEN. Mr. Stokes, we can make progress with the budget we request. I am very pleased to defend the President's budget. I think we have to make some hard internal decisions and put our money in the programs that we think will pay dividends in terms of improving the health of the American people, and that is what we are prepared to do.

Mr. STOKES. I think you are saying if you were given a little more money in this area you might be able to do a better job. Am I correct?

Dr. OLDEN. That is a fair conclusion.

ASTHMA

Mr. STOKES. I want to talk about asthma a little. We understand the incidence of asthma is increasing among children, particularly African-American children. Is that correct?

Dr. OLDEN. That is correct.

Mr. STOKES. To what extent does the environment affect the increased incidence for children, particularly African-American children?

Dr. OLDEN. We don't know the answer to that, Mr. Stokes. It is increasing among all Americans, but, clearly, it is going up much more rapidly in African-Americans than others. We would like to initiate a clinical trial. We have an outstanding pulmonary pathobiology section with basic science, and we could put that together with Duke University which has an outstanding clinical unit. The basic science at NIEHS is second to none. We are poised to make some major headway in that area.

BIRTH DEFECTS

Mr. STOKES. Dr. Olden, reading your budget justification, I see that birth defects continue to be a major concern. One out of 33 live births results in a child with a birth defect. Seventy percent of these birth defects have an unknown cause. What are some of the findings in this area?

Dr. OLDEN. If we go back to lead and mercury, that is certainly part of the explanation. There is evidence that spontaneous abortion and developmental abnormalities are associated with lead exposure and the same with the mercury.

There are probably a number of other environmental factors that one can now associate with development. I think now we can make headway in that area. I would think metals are the thing that comes to mind.

Mr. STOKES. What level of funding and staff will support research in this area in fiscal year 1993?

Dr. OLDEN. It is $7,000,000, Mr. Stokes. That is what we have requested.

Mr. STOKES. How does this compare with fiscal year 1992?

Dr. OLDEN. It is about the same. We have $6,900,000. Some of these priorities have shifted since my arrival. I think we have to make internal changes in our budget to do some of the things we need to do. They are top priorities with us.

IMPACT OF ENVIRONMENT ON IMMUNE SYSTEM

Mr. STOKES. There appears to be increasing awareness that environmental agents can cause subtle changes in the immune system processes resulting in an increasing frequency and severity of certain diseases and infections and cancer. Are you telling us anything about that?

Dr. OLDEN. UV light exposure comes to mind. We have a Shannon Awardee who has published data showing that exposure to UV light suppresses the immune system.

Mr. STOKES. What are some of the other common environmental agents which adversely affect the immune system? Are there some others?

Dr. OLDEN. Yes. Certainly exposure to UV light is one that suppresses the immune system. I think any chemical that really acts with the endocrine system may affect immunity because of the integration between the various systems.

MINORITY PROGRAMS

Mr. STOKES. Can you give us some idea, Doctor, since you have come on in the capacity which you now occupy, as to any minority-specific research and training activities you plan for fiscal year 1993?

Dr. Olden. We are recruiting for an associate director to direct minority programs for the Institute. We are currently supporting the MARC Program and MBRS. We are also supporting the National Cancer Institute's Science Enrichment Program. We have some minority supplements to RO-1 grants. In fact, we have 10 to 15 of those. So we are supporting the various minority programs that are in place at the moment.

We plan to work with Dr. Healy's office—with Dr. John Ruffin—to develop our lead initiative. While all the activities will not be directed toward minorities, a fair amount of the activities will be. Also, a portion of the asthma research effort will focus on minorities in inner cities, and we will work with Dr. Ruffin in that regard.

We also have a summer program at the Institute where we brought in 99 students last year from throughout the U.S. We brought in high school teachers from the North Carolina area and college teachers from women's and minority colleges. We have that program again this year. We should have over 100 students in it.

Those are the activities we have ongoing. It is my feeling that we need some new innovative programs to get more minorities into the mainstream. Those are the kinds of things that I am having discussions with Dr. Ruffin about.

When we get somebody on board to deal with that, those are the kinds of things I will ask them to do. I envision we will try to identify some of the RO-1 applications that missed the pay line by 10 or 20 points and try to do something to strengthen these programs so that they can compete in the mainstream.

That is the kind of program that I am interested in, Mr. Stokes.

Mr. Stokes. I am pleased to hear you say that. You are expressing some of my own concerns. Notwithstanding the Office of Minority Health, it is our feeling—and I have had extensive discussion with Dr. Healy about this—each of the institutes has the responsibility to develop their own minority programs outside of the Office of Minority Health itself. I think your thinking is right in line with ours.

Thank you very much.

Thank you, Mr. Chairman.

NEW BUILDING CONSTRUCTION

Mr. Natcher. Doctor, exactly when will the additional funds for the building—$10,000,000 down, $62,000,000 is the cost. We will need an additional $52,000,000. When will the additional funds be necessary?

Dr. Olden. I would say next year certainly we could efficiently utilize $10,000,000. That brings us back to what you suggested for us last year. The House recommended $17,800,000. It brings us back to that mark.

Mr. Natcher. Is there any money in the budget that we have before us for this construction?

Dr. Olden. No.

SUPERFUND

Mr. NATCHER. How much additional money does your Institute get from other sources, Doctor, such as the Superfund, and how has this changed over the years?

Dr. OLDEN. We are currently getting $51,000,000 from the Superfund trust for research and workers' training.

What was the second part of the question?

Mr. NATCHER. Over the years, how has it changed as far as amounts are concerned?

Dr. OLDEN. It has grown from $13,000,000 in FY 1987 to the current amount of $51,000,000.

CHANGES IN FY 92 FUNDING LEVELS

Mr. NATCHER. There appears to be a number of significant changes in your 1992 spending plan compared to the budget that was presented a year ago. We are particularly interested in the changes for grants and contracts. What can you tell us about this shift?

Dr. OLDEN. We were able to fund more research grants because of the transfer of some $3,000,000 from the National Cancer Institute. We decreased contracts by about $4,000,000, and that was due to a salary and expense reduction by the Department. We took that cut out of contracts.

RESEARCH TRAINEES

Mr. NATCHER. As you know, the mechanism table on page 111 shows a reduction in the number of trainees from 556 in 1991 to 455 in 1992 and 1993. Are these numbers accurate?

Dr. OLDEN. Yes, they are. I asked about that. That number fluctuates on a year-to-year basis depending on the number of traineeships, the number of institutions that attract trainees to the program. Some years there are more and others there are fewer, and we have monies left over. The number stays around about 450 to 500.

But in some years it might go up as high as 550, as you indicated.

Mr. NATCHER. Last summer the Institute of Medicine recommended that the government take immediate steps to increase the number of physicians trained in environmental medicine. Does the 1993 request address this problem?

Dr. OLDEN. We have not requested new funds for that activity. We are now supporting about 10 grants in that area to increase environmental health and science education in the medical school curricula in various medical schools. So we have 10 awards, and that is what we will have for 1993.

FY 92 STAFFING INCREASE

Mr. NATCHER. The mechanism table shows an increase of 15 full-time positions in 1992, which were not discussed with the Committee. What can you tell us about this additional staff, Doctor?

Dr. Olden. We created a new laboratory in carcinogenesis and we had to staff that group. In addition, I brought in some new people with my appointment; that probably accounts for 15 overall.

Mr. Natcher. Doctor, you are new. You will find that Mr. Stephens, who sits here on my right, is very much concerned about these matters. You are going to please him in the future if you don't to surprise him.

Dr. Olden. I won't surprise him.

USE OF NON-ANIMAL MODELS

Mr. Natcher. Both the House and Senate have expressed concern about the use of animals in toxicology studies. What progress is being made in developing non-animal models?

Dr. Olden. We have research going on looking at least three alternatives: fish, amphibians and fruitflies. I am told the progress looks very good that we can use amphibians for developmental toxicology.

TOXICOLOGY PROGRAM

Mr. Natcher. What mechanism is used for funding in the toxicology program, grants or contracts?

Dr. Olden. Primarily contracts.

Mr. Natcher. Do you expect any change in the way these programs are being run as a result of the environmental council review?

Dr. Olden. I don't know to what extent, but I do expect some changes. Two activities are going on now. I asked the executive committee for NTP to take a look at the program and make some recommendations as to what needs to be done.

For example, I was concerned, since in 1981 we had 54 chemicals starting on long-term chronic tests but in 1992, we will start eight long-term tests.

So that is a dramatic decrease. I think if we are going to only test eight per year, we have to be certain we are testing the eight that have the largest impact on human health. I want to be sure that our selection process does identify the most hazardous chemicals.

I also want to ask the Committee to take a look at how we communicate the results to other Federal agencies and also to the public. I also asked the Committee to see if we are doing enough on mechanisms, because I think mechanisms are what it's all about.

It is one thing for me to come tell you every year that I have identified seven or eight agents that are toxic to human health, but I think it would be better for the American people if I had some information on mechanisms, because that will allow us to intervene and save lives and money.

So in addition, I have asked the senior leadership of the Institute to take a look at the intramural organization. Toxicology has evolved in recent years into an interdisciplinary science depending not only on toxicology but also mathematical modeling and molecular biology.

Mathematical modeling is in one division and toxicology is in another division and molecular biology is in a third. The communication among the three is not adequate in my estimation. I think we need to get rid of the artificial barriers so we can get the communication to improve the science not only of NTP but risk assessment and also our basic science program.

So my objective is to improve the quality of the science so we can do better risk assessment. I think probably as a Nation we are spending a lot of money regulating chemicals simply because we don't have adequate information.

NATIONAL TOXICOLOGY PROGRAM FUNDING HISTORY

Mr. NATCHER. If you will insert in the record a 10-year history of funding for the toxicology program, Doctor. Place it in the record at this point.

[The information follows:]

National Toxicology Program

History of Funding

Fiscal year:	
1983	$71,890,000
1984	77,265,000
1985	78,153,000
1986	76,984,000
1987	78,738,000
1988	80,522,000
1989	83,976,000
1990	82,076,000
1991	81,130,000
1992	81,855,000

RESEARCH CENTERS

Mr. NATCHER. Let me ask you a question about the research centers supported by your Institute. How many are there and what kind of work do they do?

Dr. OLDEN. There are a total of 17 centers: 12 environmental health science centers and five marine fresh water science centers. The centers, each of them, have specific focuses.

I would say overall, the major contributions have been in the area of metals, metal mercury and lead, agricultural chemicals and air pollution. As you know, we created a center in Iowa to deal specifically with agricultural chemicals.

Mr. NATCHER. Why have they been essentially level-funded for the past five years?

Dr. OLDEN. Mr. Chairman, I think that what has happened to our center is what I think has happened to centers throughout the National Institute of Health. That is, centers as a mechanism of funding are not accorded the same kind of priority in the scientific community—and in Congress. We protect the RO–1 line. In order to do that in time of shrinking resources, centers have not grown at the rate that we wish they would have.

But I think it is simply a lack of appreciation, that a center is appropriate and desirable, in some cases—a proper mechanism for funding research. Particularly, it gives the researchers an interdisciplinary approach in areas such as environmental health or cancer.

AIR POLLUTION AND ASTHMA

Mr. NATCHER. During our time with the directors at the NIH, we have discussed asthma with them. Can you tell us whether air pollution has an impact on asthma?

Dr. OLDEN. We certainly think so. I mentioned in my opening statement that I convened an ad hoc advisory committee to look at that.

We are developing our work with the National Institute of Allergy and Infectious Diseases and the National Heart, Lung and Blood Institute, since they conduct research in that area. It was the conclusion of the ad hoc committee that there is a component that is caused by the pollution in the atmosphere and we have a responsibility, in fact, to address that issue.

COST OF CENTRALLY-FURNISHED SERVICES

Mr. NATCHER. The table on page 18 of the justification shows a 13.5 percent increase in the cost of centrally-furnished services. Why are these costs increasing so rapidly, Doctor?

Dr. OLDEN. It is going up, but that is the NIH management fund and I think those are costs that they experience due to inflation.

FUNDING HISTORY

Mr. NATCHER. Now, Doctor, if you will, place in the record at this point a 10-year table showing the appropriation for the National Institute of Environmental Health Sciences, the dollar and the percentage change over the previous year, and the percentage change for NIH as a whole. Also include a column showing the total budget of the Institute showing reimbursables, with the dollars and the percentage change. If you would place that in the record for us, we will appreciate it.

Mr. Stokes, I yield.

[The information follows:]

National Institute of Environmental Health Sciences

Appropriations History

(Dollars in thousands)

	NIEHS			NIH	NIEHS		
Year	Appropriation	Change over Prior Year	% Change over Prior Year	% Change over Prior Year	Appropriation plus Reimburseables	Change over Prior Year	% Change over Prior Year
1983	$164,867				$165,734		
1984	180,597	$15,730	9.5%	11.7%	181,520	$15,786	9.5%
1985	194,819	14,222	7.9%	14.6%	197,755	16,235	8.9%
1986	188,986	-5,833	-3.0%	2.2%	195,918	-1,837	-0.9%
1987	209,294	20,308	10.7%	17.5%	227,799	31,881	16.3%
1988	215,666	6,372	3.0%	7.8%	235,521	7,722	3.4%
1989	223,454	7,788	3.6%	7.3%	251,160	15,639	6.6%
1990	229,234	5,780	2.6%	5.9%	270,455	19,295	7.7%
1991	241,028	11,794	5.1%	9.2%	286,312	15,857	5.9%
1992	252,031	11,003	4.6%	8.0%	305,939	19,627	6.9%

MINORITY EMPLOYMENT

Mr. **Stokes**. Doctor, being new to the Institutes, I know that you have inherited a staff there. You have, what, about 546 permanent?

Dr. **Olden**. We have 714, I believe the number is, full-time equivalents, FTEs.

Mr. **Stokes**. I was looking here at the page where they have detailed permanent positions. Is that part of that?

In your detailed of permanent positions, there are 546, correct?

Dr. **Olden**. Yes.

Mr. **Stokes**. You have ES positions, ES–5, –4, –3, GS–14, –13, –12, et cetera. Have you looked at your staff from the viewpoint of minority employment?

Dr. **Olden**. Yes, I have, Mr. Stokes. Right now, we have a total of 220 minorities. I don't have the total breakdown, but 173 of those, I think, are African-Americans, and I believe, two are Native Americans. Roughly, 25 percent of our staff are minorities.

Mr. **Stokes**. Are they spread across all of your grade levels?

Dr. **Olden**. They are spread across the grade levels, but obviously there is a skewing toward the lower GS range.

Since I have been there, I promoted with Dr. Healy's approval, a Hispanic to an SES position, and granted tenure to a Native American. This is something, Mr. Stokes, that we are clearly concerned about.

We think when we come back here in future years, the numbers will be different. We have 12 black Ph.D.'s; one of those was tenured when I arrived and one has been tenured since my arrival. We are making every effort to have mentorships within the Institute, so minorities will develop their potential and get tenured. We are very concerned about that.

Mr. **Stokes**. I am pleased to hear that you are concerned.

I would like for you to expand on the record in terms of giving me the precise information and data with reference to each minority group and what positions they hold throughout the Institute. You might expand in terms of both what you have done since you have been there and your anticipatory plans.

[The information follows:]

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES—MINORITY PERSONNEL

	Black	Hispanic	Asian	Native American	Total
Research/Support:					
SES	1	1	0	0	2
GS/GM 15	0	0	3	0	3
GS/GM 14	1	0	2	0	3
GS/GM 13	5	0	1	1	7
GS 12	6	0	1	0	7
Other	149	5	5	1	160
Visiting Programs	8	2	21	0	31
Experts	2	0	0	0	2
IRTA's	1	1	3	0	5
Total	173	9	36	2	220

Dr. OLDEN. I think when we get the associate director to help us out with those activities, we will see dramatic progress. That is why we are bringing that person aboard at that level, to demonstrate our commitment.

Mr. STOKES. We look forward to that.

Mr. NATCHER. Dr. Olden, we want to thank you and your associates for appearing before the Committee at this time on behalf of your budget request for fiscal year 1993. You have handled this very well. It pleases Dr. Healy and me when you do this.

[The following questions were submitted to be answered for the record:]

ENVIRONMENTAL EQUITY

Mr. Stokes: As noted in the 1985 Heckler Report, African Americans suffer from a disproportionately high rate of disease compared to whites. Some suggest that environmental factors contribute to this disparity, e.g., location of hazardous waste sites, industrial exposures, pollution, etc. I understand that NIEHS is planning to hold a conference this year on environmental equity. This is an issue in which I have been interested for a long time. In fact, I addressed it last year with your Institute. What will be the nature of this conference and what aspects of this issue will be addressed?

Dr. Olden: NIEHS is co-sponsoring a conference on Environmental Equity with the Environmental Protection Agency and the Agency for Toxic Substances and Disease Registry. The goal of the conference is to identify research needed to characterize differences in exposure to and health consequences from environmental agents in minority, economically disadvantaged, and non-disadvantaged communities by reviewing the history and current understanding of differences in potential sources of and exposures to environmental pollution; reviewing relevant data on disparities in health status related to environmental exposures; identifying current research activities directed toward these issues; and determining and setting priorities for future research in response to inequities. The conference will be held in two parts: In August 1992, a workshop will be held in the Research Triangle Park, NC, area. Researchers will be invited to participate in four media oriented workgroups---air, water, pesticides/food, and hazardous waste, and crosscutting areas such as biological susceptibility and data collection issues. In December 1992, a large symposium will be held in Washington, D.C., at which time the draft workshop papers will be submitted to a much larger audience of interested participants who will have opportunities to critique and discuss them.

Mr. Stokes: What progress has been made in developing better biomarkers of exposure and effects?

Dr. Olden: Developing sensitive and specific biomarkers for monitoring and quantifying human exposure to environmental or occupational agents is one of the highest priorities of NIEHS. The acquisition of exposure data through analysis of cells, tissues, or body fluids of exposed people has the potential to identify hazardous exposures before adverse health effects appear, and to establish exposure limits to minimize the likelihood of significant risk. Recent biomarker research lead to the discovery that aflatoxin B_1, a potent carcinogen found in moldy agricultural feed, binds to DNA and proteins and can be measured to indicate the dose that an exposed individual has received. A number of chemicals such as methylene chloride, chlordane, and trichloro-ethylene have been shown to activate genes that cause cancer. The presence of these "oncogenes" in tissues of potentially exposed persons confirms that exposure has occurred. The identification of receptor mediated testicular toxicity from the industrial chemical mono(2-ethylhexyl) phthalate, and the interaction of dioxin with the aryl-hydryl receptor also provide physicians with positive proof that an individual has been exposed to these harmful agents which provides for earlier detection of exposure and diagnosis.

Mr. Stokes: To what extent has the Institute identified effective approaches to address the public health issues which have been raised as a result of questions surrounding environmental equity?

Dr. Olden: NIEHS's involvement in the issue of environmental equity has traditionally been in the areas of identifying risk groups, conducting research to lead to prevention of exposures, and developing treatment strategies once exposure has occurred. There are a multitude of issues which have been identified as possible contributors to poor minority health such as proximity to industrial plants and hazardous waste sites and occupational risks. Additional research is needed to investigate the interaction of these risk factors with others, such as poor nutrition and inadequate access to health care. The conference on environmental equity planned for later this year will help to identify the research gaps and information needed to once and for all identify which of these issues are indeed contributing to poor health and the proper public health interventions to ameliorate them.

LEAD

Mr. Stokes: Lead poisoning remains the most common and devastating environmental disease of young children. It is estimated that about 17 percent of our nation's children, six months to five years old, living in metropolitan areas, are exposed to environmental sources of lead at concentrations which place them at risk of adverse health effects. The consequences of lead poisoning are all the more deplorable because they are completely preventable. How does nutrition impact the effect of lead on children?

Dr. Olden: Nutrition interacts with and affects the toxicity of lead in many and complex ways. Major nutritional components in this interaction are iron, calcium, protein, fat and vitamins. Processes affected include uptake, absorption, and distribution of lead from all sources and exposure to interactions and excretion of lead.

Lead competes with iron and calcium at many biological membranes both inside and outside the cell. Thus, low body levels of iron or calcium will be associated with more lead being available to sensitive tissues and to sites of action. Low protein and high fat in the diet also seem to "set up" the child for enhanced lead toxicity. Lead interferes with vitamin actions, and if there is vitamin deficiency, it can be made worse by lead. Thus, malnutrition of several types can be a most potent synergizer of lead toxicity, especially in children.

Mr. Stokes: To what extent does the presence of lead in a mother's body affect a fetus?

Dr. Olden: Any lead in the mother's blood can be passed through the placenta to her fetus where it can accumulate in sensitive tissues such as the brain and developing nervous system. The mother's blood lead concentrations are affected by current lead exposures and by any previously stored tissue lead, primarily in her bones. Bone lead can be mobilized into the mother's blood by stress, immobilization, or too little maternal intake of calcium, especially at times when fetal skeleton development is demanding large amounts of calcium.

CLINICAL RESEARCH

Mr. Stokes: The justification states that the Institute recognizes the need to enhance the clinical component of environmental health studies. In fact, within the last year, a director of clinical research was named. What other steps are being taken to enhance clinical research?

Dr. Olden: An effort is underway to take advantage of NIEHS' close proximity to a number of outstanding clinical research facilities by initiating a series of clinical studies that are an outgrowth of basic research conducted at the Institute and that are concerned with human diseases and disorders that have a known or suspected environmental component. In addition, individual Institute investigators are continuing to pursue one-on-one research collaborations with clinicians both in the immediate area and throughout the country. A series of workshops or consultations are being conducted with leading members of the extramural scientific community to prioritize the clinical research activities in which NIEHS will be involved in the future.

Mr. Stokes: What types of activities are being supported?

Dr. Olden: Among the various research activities likely to be supported under the proposed NIEHS Clinical Program are clinical studies designed to identify different biological mechanisms that are important in triggering or aggravating various forms of asthma with particular emphasis on those related to environmental factors, and based on that knowledge, to develop new strategies of disease prevention, intervention and management; to evaluate osteoporosis and bone density changes in women who have experienced prenatal DES exposure as a clinical follow up to recent NIEHS findings in mice describing adult bone density changes due to prenatal and neonatal DES exposure; to evaluate childhood lead poisoning treatments, including chelation drugs and nutritional supplementation with vitamins and minerals such as Vitamin D, iron, and calcium; and to evaluate the environmental contribution to neurodegenerative diseases such as the role of aluminum in Alzheimer's disease. We are continuing our clinical studies on precocious puberty.

Mr. Stokes: What level of funding and staff are being requested for this program in FY 1993?

Dr. Olden: The President's Budget request includes approximately $3.7 million and 8 full-time equivalent personnel for these activities.

Mr. Stokes: How does this compare to levels provided in FY 1992?

Dr. Olden: In FY 1992, we will spend approximately $2 million and use approximately 6 FTEs.

MINORITY EFFORTS

Mr. Stokes: I am pleased to see the appointment of Dr. Olden as the Director for NIEHS. I am curious, however, as to how many and what percentage of employees of your Institute are minorities.

Dr. Olden: We have 220 minority employees. That is approximately 25% of our total employees.

Mr. Stokes: How many are employed in a research capacity?

Dr. Olden: We employ 96 minority researchers. In addition to these scientists, we have 92 minority employees in the Intramural activity who provide support to our researchers.

Mr. Stokes: Please describe for the Committee the resources and funding levels which will be provided for minority-specific research and training activities in Fy 1993.

Dr. Olden: In FY 1993 we plan to spend approximately $8.1 million on minority health research, $650,000 on minority extramural training, and $206,000 on minority intramural training.

Mr. Stokes: How do these levels compare to last year's levels?

Dr. Olden: In FY 1992 we are spending approximately $7.8 million on minority health research, $637,000 on minority extramural training, and $190,000 on minority intramural training.

Mr. Stokes: The total funding represents what percentage of your budget?

Dr. Olden: This represents about 3.4 percent of our budget.

Mr. Stokes: To what extent are you working with the Office of Minority Health to effectuate these goals?

Dr. Olden: NIEHS has and will continue to work closely with the Office of Minority Programs (OMP) to improve the health status of minorities and support minority training initiatives. I have accepted an invitation to participate in the Minority Health Roundtable sponsored by the OMP. We have responded to the OMP on a number of requests for information on NIEHS minority health and training efforts. The Office of Minority Programs will be invited to participate and take an active role in the upcoming conference on Environmental Equity.

RESEARCH PROGRAMS

Mr. Early: Your predecessors and I have discussed whether there was a need for a clinical research program at NIEHS. So, I am pleased to learn of your initiative on clinical studies. How are your plans for studies in pulmonary medicine and childhood lead toxicity progressing.

Dr. Olden: Separate one day meetings involving leading experts from the extramural scientific community and NIEHS personnel have been held at the Institute to solicit their advice about how the Institute might most effectively address these clinical issues. The Institute is now in the process of developing requests for procurement (RFP) that will lead to the initiation of clinical studies designed to identify different biological mechanisms that are important in triggering or aggravating various forms of asthma,and to evaluate childhood lead poisoning treatments, including chelation drugs and nutritional supplementation with vitamins and minerals.

Mr. Early: Do you have adequate resources?

Dr. Olden: The President's request contains approximately $3.7 million for these clinical research programs.

Mr. Early: We know that prevention is the cornerstone of good health. Will you be able to get started in FY 1992 on some of these projects?

Dr. Olden: Allow me to elaborate on my earlier remarks pertaining to prevention research. Historically, research on hazard identification, risk assessment, susceptible populations, and routes of transmission at NIEHS has made up about 80 percent of our budget. This research is related to and in support of prevention of illnesses. The Centers for Disease Control, local public health organizations, and federal regulatory agencies use the results of our research in their prevention programs such as regulating levels of chemicals in ambient air and water, community education to prevent lead poisoning, monitoring the work place for safe levels of chemicals, and so forth. My vision is for NIEHS to continue to supply the information needed by these other agencies, but also, to move into the area of performing and evaluating prevention programs. I have appointed a senior member of my staff to incorporate what is known about environmental agents, routes of transmission, and the people who are susceptible into comprehensive prevention programs which will lead to real improvements in public health. An example is the lead demonstration project we are planning for later this year which will evaluate methods for reducing exposure to lead found in soils and household dusts.

Mr. Early: Is there funding in the President's request for FY 1993?

Dr. Olden: There is enough flexibility in the request to strengthen the comprehensive prevention programs.

Mr. Early: The National Advisory Environmental Health Sciences

Council convened a task force on research needs and opportunities in the area of environmental health. What recommendations did the task force make?

Dr. Olden: The following are recommendations, as included in the executive summary, pages 20 and 21 of the task force report:

Summary and Conclusion - Scope of NIEHS Research and Training

The NIEHS mission, while exceptionally broad, is not universal and, in an age of limited resources, must necessarily focus on research strategies and specific targets that will achieve the greatest degree of public health protection. Some of the guiding principles adopted by the Task Force in preparing its recommendations were:

1) The primary objective is to prevent adverse effects resulting form exposure of the general population to environmental toxicant. Such exposures can be direct, e.g., through ambient air or drinking water, or indirect, through the consumption of foods containing toxicant originating from a variety of sources.

2) Effective and efficient prevention programs depend on knowledge of the mechanisms by which: a) humans are exposed to toxicant; and b) biological processes lead to acute and/or cumulative damage and disease.

3) Knowledge of the mechanisms of exposure and biological response provide the means for developing intervention strategies that can reduce excessive exposures, and/or prevent early biological changes from progressing to functional impairment and disease. Such knowledge may also identify individuals or population subgroups that are particularly susceptible to a hazardous agent.

4) NIEHS is a natural focus for research that defines the nature and scope of the impacts of environmental toxicant on human health. Nevertheless, it cannot effectively address all of the research problems that it identifies solely with its interests in specific areas, and the fruits of their research programs are of direct interest and benefit to NIEHS, especially in molecular biology and epidemiology. More proactive research planning and coordination among the Institutes would be highly desirable. Similarly, NIEHS has many common interests with agencies outside NIH, such as EPA, FDA,

NIOSH, ATSDR, NCHS, NOAA, DOE, etc., an NIEHS should seek to broaden the coordination of research in areas of common interest with these agencies.

5) NIEHS can exert a greater leadership role in environmental health research by developing a new framework for research planning based on a formal mechanism for risk assessment that would consider both incidence and severity of impact. This would differ from conventional risk assessment as used for regulatory purposes, and would focus on the identification of

critical knowledge gaps that currently limit our ability to do both relative and absolute risk rankings of environmental toxicants.

Two of the major knowledge gaps currently limiting relative risk rankings are interspecies extrapolation and high-dose-to-low-dose extrapolation. The rapidly increasing data base on molecular mechanisms of toxicant damage and the development of biomarkers for such damage create new opportunities for productive research on human subjects that would address these needs. Thus, NIEHS should consider undertaking a major initiative in clinical and epidemiological research to complement its strong research program in toxicology.

6) Remarkable progress in the past decade in biophysical methods can provide three-dimensional information on interactions of environmental toxicants with the human host. Similarly, the impressive advances in molecular genetics offer unique opportunities to understand human responses to toxicants. Now is a particularly opportune time to increase NIEHS intramural and extramural efforts in these areas since such enhanced understanding is the key to future prevention and intervention strategies.

7) To staff the broadened research program that is called for will require a substantial increase in professional training, with programs in newly emerging areas such as environmental epidemiology, exposure assessment, and clinical environmental medicine, as well as sustained support for more traditional NIEHS programs in toxicology, biochemistry and pathology.

The recommendations of the Task Force address needs and opportunities that range beyond areas in which NIEHS has had strong and productive programs, into areas that have not previously been investigated in depth. For example, the success achieved in understanding of the dosimetric and mechanistic processes affecting disease in laboratory animals has created opportunities for new initiatives in clinical and epidemiological research.

Mr. Early: Are there new funds in your FY 1993 budget request to implement any of these recommendations?

Dr. Olden: The recommendations were in line with the current priorities of the Institute.

Mr. Early: How would you prioritize these recommendations?

Dr. Olden: The authors of the Task Force Report narrowed the scope of their effort to identify environmental health problems of greatest national significance and to areas of environmental health sciences research that are ripe for application to the problems. In so doing the Task Force established priorities for environmental health sciences research which I accept as valid and have incorporated into my vision for NIEHS.

Mr. Early: Would you bring me up to date on your Superfund basic research program.

Dr. Olden: The NIEHS Superfund Basic Research Program received $30.615 million for FY 1992. This is separate from the $20.5 million received from EPA for the Worker Safety Training Program that is used to train workers who are actively involved in site remediation. The Basic Research Program funds research investigating the public health implications of Superfund sites such as groundwater contamination, tracking, monitoring, and modeling the movement of chemicals from these sites into plant and animal species, and investigating methods for remediating hazardous waste sites. All research programs were reviewed by a peer review panel in 1991. Participating universities and new grantees will begin the second phase of their work on April 1, 1992. NIEHS will then be supporting 130 hazardous waste health research projects at 18 universities.

Mr. Early: What progress is being made in identifying ways of dealing with hazardous waste?

Dr. Olden: Bioengineering of organisms for degradation of hazardous substances can provide a less expensive and less physically disruptive method for remediating waste sites. The number of identified hazardous waste sites in the U.S. grows daily; however, the remediation and clean-up activities cannot keep pace. Also, the cost of the clean-up for each site can reach several million dollars. Scientists are investigating the ability of genetically altered white rot wood fungus to biodegrade certain hazardous substances such as trinitrotoluene. Other investigators are genetically manipulating the metabolic activities of microbial organisms so that they may metabolize volatile organic compounds into inert substances. Environmental engineers and microbiologists have also made progress toward optimizing a "bioreactor" which utilizes sequential treatment with anaerobic and aerobic bacteria to degrade halogenated organic chemicals that frequently contaminate groundwater.

Mr. Early: The NIEHS was given certain responsibilities under the Clean Air Water Act amendments of 1990. Would you summarize your program plans for this area for FY 1992 and FY 1993?

Dr. Olden: NIEHS and EPA are holding a series of workshops to identify and set priorities for key research needs related to the Clean Air Act. The first workshop, held in March 1991 was on chronic ozone exposure and has resulted in NIEHS developing a request for applications soliciting research proposals relating to the mechanism of action of ozone, the possibility of a threshold, and the synergistic action of ozone with other common environmental pollutants. Future joint workshops will consider the health effects research needs in the areas of acid depositions and precipitation, air toxics, and global warming in anticipation of the resources needed to carry them out.

NIEHS has convened a group of experts on mercury toxicity to aid in its report to Congress on possible threshold levels, as required in the Clean Air Amendments. The first meeting was held in January 1992 and a draft document was written which is being circulated among the participants. A final report is expected this year.

Mr. Early: Are there sufficient funds in your budget request for this purpose?

Dr. Olden: NIEHS currently spends $35 million on all forms of air pollution research. This research covers most of the activities mentioned in the Clean Air Act.

Mr. Early: Last year you indicated that a final review was in process to determine research needs and information gaps in the understanding of the health effects of air pollutants. What recommendations came out of this review?

Dr. Olden: The recommendations were that more research is needed on the health effects o ambient ozone and td carry out investigations into the possible contribution of air pollutants in the development of asthma.

Mr. Early: When, and how, do you plan to implement these recommendations?

Dr. Olden: The ozone workshop mentioned previously resulted in the development of a request for applications. Awards should be forthcoming during FY 1992. Plans for additional asthma research are being developed. In February 1992 NIEHS convened a group of clinicians and researchers investigating causes of asthma. This group recommended that NIEHS conduct epidemiologic and field investigations to determine high risk groups such as children, the aged, and pregnant women and identify specific pollutants that exacerbate the development or effects of asthma and at what level of exposure. A research plan to address these recommendations is currently being developed. It will contain research and clinical components that will be carried out both intramurally and extramurally.

Mr. Early: I understand that a new drug, dihydrexidine, may hold some promise in treating Parkinson's disease. What can you tell us about this new drug?

Dr. Olden: After extensive testing in rodent models, dihydrexidine was administered to monkeys with induced Parkinson's disease. In controlled studies, dihydrexidine resulted in a dramatic reduction in parkinsonian signs, essentially making the monkeys normal in appearance while the drug was present.

Mr. Early: A new class of chemical receptors, "orphan receptors", has been identified. Why is this finding important?

Dr. Olden: As these orphan receptors are identified, new possibilities for research are opened. The foreign chemicals that interact with these receptors cause cancer, birth defects, reproductive toxicity, neurological, and other abnormalities in rodents and possibly humans. By comparing the receptors in rodents and humans, we can better predict from rodent studies the impact of these chemicals on humans and the exposure levels that may be hazardous. We can also devise new strategies for possibly blocking the effects of toxic chemicals and for treating diseases. Finally, and perhaps most importantly, many human diseases, including cancer, birth defects, and neurological disorders, have no known causative agent. The possibility exists that the physiological molecules that bind to these receptors have, on rare occasions, abnormal effects on cells resulting in health defects.

Mr. Early: A new topic of research for NIEHS is "Environmental Equity". What can you tell us about this new area of research?

Dr. Olden: Environmental Equity refers to an equal sharing of the burden of environmental problems such as municipal and hazardous waste sites, industrial complexes, and occupational exposure by all socioeconomic and racial groups. All to often minority and poor populations have a disproportionate share of this burden placed on them because landfills and hazardous waste sites are located in and around their neighborhoods, and because they are employed in jobs where their potential for exposure to noxious agents is greater than more affluent groups. The role NIEHS can play in this issue is to determine what adverse health effects are attributable to the lack of environmental equity and find ways to prevent exposures, develop treatments or interventions once exposure has occurred, and to educate the public about what they can do to protect themselves.

Mr. Early: What are your program plans in this area of research?

Dr. Olden: NIEHS has long supported a number of research projects that address environmental inequities such as lead exposure in inner city children and the adverse health effects of pesticide exposures in migrant farm workers. We are planning to conduct a local community based demonstration project on lead poisoning prevention during the coming year. Also, NIEHS has agreed to co-host a two-part conference on environmental equity with the Environmental Protection Agency and the Agency for Toxic Substances and Disease Registry to be held in August and December of this year. The goal of the conference is to determine the research needed to characterize differences in exposure to and health consequences from environmental agents in minority, economically disadvantaged, and non-disadvantaged communities and to set priorities for future research in response to inequities.

Mr. Early: Last year, you also told us that NIEHS was initiating a program to develop the area of environmentally and occupationally induced diseases in medical school curricula. Bring us up to date on this program, if you will.

Dr. Olden: The NIEHS has successfully initiated the environmental and occupational medicine academic award program over the past two years by making 8 awards. In the 1993 President's Budget, it was possible to offer 2 more awards. The 10 awardees all have as a major goal to strengthen the environmental and occupational medicine curriculum at their medical schools. They will meet each year to coordinate their efforts, and the next meeting will focus on how to accomplish their learning objectives. One of their ultimate goals is to develop a core curriculum that will be available to other medical schools. In this way, the award will serve to strengthen the environmental/ occupational medicine curriculum at medical schools beyond the awardees' home institutions and eventually instill an appreciation of environmental medicine into newly trained clinicians throughout the country.

RPG'S - AVERAGE COST INCREASE

Mr. Early: What was the downward adjustment rate for noncompeting and competing grants in FY 1991 and FY 1992?

Dr. Olden: During FY 1991, the NIEHS undertook the process of reducing its commitments on both competing and noncompeting grants. Noncompeting grants were adjusted in the aggregate by 14% and subsequent noncompeting years were adjusted from this level. The overall portfolio of competing grants was adjusted by about 15%.

During FY 1992, we do not plan any adjustments to our noncompeting grants. However, the aggregate base of our competing grant portfolio is being adjusted by approximately 16% in order to meet the dollar and number targets for the fiscal year. This adjustment is being achieved through close scrutiny of the individual projects selected for payment, the expressed needs of the applicant and the likely contribution of the individual project to the overall scientific mission of the NIH and the NIEHS.

Mr. Early: What are you projecting for FY 1993?

Dr. Olden: During FY 1993, we do not anticipate making downward adjustments to our noncompeting grants in keeping with the policies expressed in the NIH Financial Management Plan. However, as in FY 1992, a similar aggregate adjustment of about 18% to competing grants may be required for the year. Such a reduction would be performed through continuation of our current practice of closely monitoring requested costs and negotiating specific aims to be conducted with applicants.

Mr. Early: Will your Institute be able to fund noncompeting grants at commitment levels and new and competing grants at peer reviewed levels?

Dr. Olden: As I previously indicated, we plan on meeting our noncompeting commitments. While we do not currently anticipate being able to fully meet the peer reviewed levels, any adjustments necessary will be undertaken based on the peer reviewers recommendations about the science and consideration of the total costs required to perform the project.

RESEARCH CENTERS

Mr. Early: What role does your Centers program play in your Institutes's mission?

Dr. Olden: The NIEHS currently supports 17 centers, of which 12 are Environmental Health Science Research Centers (EHS) and 5 are smaller Marine and Freshwater Biomedical Sciences Centers (MFB). Each of the 12 EHS Centers has a unique focus that varies with the strengths and interests of the Center investigators. For example, one Center is very strong in metals toxicology and has provided leadership in addressing health issues associated with exposure to methyl mercury in the environment, occurring as accidental exposure or through consumption of contaminated fish. Another has been a leader in studying the effects of low levels of lead on child development, while yet a third has a major focus on pesticides and their potential effect on human health. Two others have unique strengths in studies of human exposure to air pollutants, linking exposure to human health consequences. Collectively, these Centers represent a national resource of talent and leadership in addressing many of the problems that face the public with regard to environmental and occupational exposures to chemicals and other agents.

Mr. Early: Is there a need to expand your Centers program?

Dr. Olden: The highest priority for expansions to our budget are in investigator-initiated research project grants. This requires trade-offs with other Institute mechanisms. We have targeted the Centers as one of the major players in new efforts in prevention, intervention, and community outreach. Soon it will be a requirement that each Center have activities and staff in these areas, adding even a new dimension in an existing interdisciplinary collaboration. The Centers could also play a significant role in expanding the clinical activities of the Institute. Many of the existing ones are located in medical schools and contain faculty in both the basic and clinical sciences, making the "bench to bedside" transition a real possibility. Also, there are many new and exciting areas of research, such as the effects of environmental agents on reproduction and development, on the neuroendocrine system, and on the immune system, that need more attention and support.

Mr. Early: What is the average increase in a Center grant under the budget request?

Dr. Olden: The budget request for FY 1993 contains no increase for our center grants.

Mr. Early: Doctor, will you be able to fund noncompeting centers at the commitment level and competing centers at the peer reviewed level?

Dr. Olden: Since funding for the Centers program has remained fairly constant over the past few years, we are unable to support the centers at peer reviewed levels. However, there are sufficient funds in the request to continue the research effort.

Mr. Early: Is the NIEHS making greater use of "out of order" funding to achieve a lower cost per award?

Dr. Olden: Due to the small number of applications within the NIEHS portfolio, opportunities to select smaller grants are limited. We primarily try to fund the most meritorious science as indicated by the scientific merit score and then adjust budgets to still leave the research projects viable. We usually fund "out of order" based upon the importance of and need for the proposed research project's results. However, sometimes budgetary considerations will affect what we fund. For example, a very expensive study within the pay line, such as a program project or an epidemiologic study, might cost as much as five or more average research grants, and we would have some reservations about funding these.

Mr. Early: What impact is limiting the average increase in the cost per award having on your Institute's research program?

Dr. Olden: NIEHS staff are making budgetary adjustments on an individual award basis and then projecting these over the full project period of the grant. Our experience has been that these adjustments are often absorbed by reducing personnel costs on the grant.

Mr. Early: I understand that environmental epidemiology studies are rather expensive. Have you had any difficulty in this area?

Dr. Olden: We must be selective in the funding of such studies due to their costs. Sometimes we can achieve significant reductions in costs of these studies, but usually reducing costs means less sampling and therefore less statistical power in the studies or a longer period for collecting information. We also must consider appropriate compositions of the study populations with regard to women and minorities, and this can make it difficult to cut costs.

OTHER BUDGET

Mr. Early: What was the NIEHS professional judgment budget and how does it differ from the request before us?

Dr. Olden: The NIEHS request to PHS was for $300.4 million, which is $38.9 million less than the request before you. The differences cover all of our mechanisms of funding.

Mr. Early: Will any significant new research initiatives or opportunities be lost or delayed by lack of funds in the FY 93 budget request?

Dr. Olden: In comparison to the NIEHS submission to PHS, the 1993 budget request does not include expanded efforts in the development and validation of biomarkers of environmental exposures; the full development of planned clinical studies on environmental components of asthma; expanded research efforts into the neurological effects of lead and other environmental neurotoxicants; initiation of a program on the effects of environmental toxicants on birth weight, birth defects, and infant mortality; and initiation of targeted training programs to develop and encourage investigators with expertise in basic biological sciences to focus their research efforts on areas of high priority in environmental health sciences.

Mr. Early: What priorities would the Institute pursue if additional resources were available?

Dr. Olden: The Institute envisions its priorities as research related to biomarkers, asthma, neurotoxicity, fetal and infant health, environmental equity, nutrition, aging, and intellectual capital.

Mr. Early: If an increase over the FY 1993 request is provided, how would you use these additional funds?

Dr. Olden: Although we have allocated our FY 1993 resources to those areas we consider the highest priority, if additional funds were available, NIEHS would pursue additional studies on treatments and interventions in lead poisoning and asthma and other respiratory diseases. In addition more research on reproduction and development, neurologic and neuroendocrine diseases, environmental factors in immunologic disorders, and the identification of additional biomarkers of exposure and effect are areas that require more research to determine and understand the interactions of environmental factors in the development of disease. These areas of research would be incorporated and cut across the program areas of prevention and intervention, risk assessment, clinical studies, and environmental equity issues that I see as the new direction of NIEHS.

Mr. Early: For FY 1992, the NIEHS will receive $3 million for cancer research from the National Cancer Institute. How do you plan to use these funds?

Dr. Olden: How environmental factors might induce cancer is an important issue being investigated by mechanistic and epidemiologic studies supported by the NIEHS. The funds will support approximately 15 studies in this area. Already selected are studies of radon exposure and cancer incidence and a human study to follow-up on the question of fluoride exposure and osteosarcoma. Other mechanistic research grants are now being screened for funding as are several grants in the area of cancer biomarkers.

Mr. Early: The budget justification indicates that the Institute plans to increase research career awards in FY 1992. What are your plans in this area?

Dr. Olden: During FY 1992, we are awarding additional Environmental and Occupational Medicine Academic Awards. These awards are intended to expand the curricula in environmental medicine at academic institutions.

STRENGTHENING THE NATIONAL TOXICOLOGY PROGRAM

Mr. Pursell: The sole government program for testing chemicals for carcinogenicity is the National Toxicology Program. Do you have any plans for strengthening the program?

Dr. Olden: One of my major goals as the Director of the National Toxicology Program (NTP) is to assure that the program continues to serve and protect public health in the most comprehensive way by further strengthening its role as the Nation's premier toxicology research and testing program. To accomplish this goal, I have asked for an advisory review of four specific aspects of the NTP. It is to be held at a combined meeting of the NTP Board of Scientific Counselors and subcommittees of experts at NIEHS on April 14-15, 1992. At this meeting, committees will review current programs and make recommendations on how to improve the quality of chemicals nominated for testing by assuring that they have the greatest public health significance; how to assure that emphasis is placed on studies of the biochemical and genetic mechanisms of toxicity and carcinogenicity; how to develop and validate current procedures and assays that might reduce the need for long-term testing in animals; and how to improve the procedures for alerting regulatory agencies and the public about test results on chemicals--- particularly data which suggest potential hazard to humans from chemicals of widespread importance.

STREAMLINING OF THE NTP

Mr. Pursell: Do you envision any streamlining of the NTP or more efficacious management?

Dr. Olden: Based upon the reviews and recommendations that will take place at the NTP Board of Scientific Counselors meeting in April, various NTP functions, activities and management may be modified. Reviews will focus on the nomination process, assuring that emphasis is placed on studies of the mechanisms of toxicity and carcinogenicity, developing and validating better assays to reduce dependence for long-term testing in animals, and releasing of NTP study results.

NTP SELECTION PROCESS

Mr. Pursell: Regulatory agencies depend on the outcome of NTP testing, how does the selection process serve those agencies and will there be any changes in the selection process?

Dr. Olden: The regulatory agencies will continue to have a major role in selection of chemicals nominated for testing by the NTP. Their input is achieved through their membership on the Chemical Evaluation Committee and the NTP Executive Committee. In addition to general nominations of chemicals to study, each regulatory agency may designate one chemical per year for which the NTP will expedite testing to better serve the needs of the regulatory agencies. No major changes in the selection process are anticipated. However, it is expected that there will be more emphasis on structure-activity relationships and steric considerations to help select chemicals for testing. It is also expected that more emphasis will be placed on non-cancer endpoints and mechanistic studies since such information will allow regulatory agencies to better use NTP data for regulatory purposes.

MECHANISTIC STUDIES ON CARCINOGENESIS

Mr. Pursell: Are you considering mechanistic studies on carcinogenesis to complement the program?

Dr. Olden: I do envision some increased emphasis in mechanistic studies on carcinogenesis. At a review of the NTP in April, I have asked the Board of Scientific Counselors to address some important questions for me regarding mechanistic studies. They will be addressing questions such as the following: Within the various specialty areas of toxicology, can you suggest high priority areas of mechanistic research which would lead to improvements in the risk assessment process? How much of our efforts should be committed to evaluating the accuracy of animal models rather than chemical evaluation? Compared to our current balance between screening and in-depth research efforts, would the NTP make more of an impact by concentrating our resources on a smaller number of chemicals or issues? Considering the broad scope of toxicology, should the NTP have a very small number of areas of emphasis where we want to be the leaders or should we be involved in a wide range of areas but not expect to be a world-center in any of them? Should we be a world-center in multiple areas? What factors should be considered in selecting a specific area of research? The Board's responses will assist me in formulating future plans for mechanistic studies in the NTP.

ANIMAL ALTERNATIVES

Mr. Pursell: Are you considering the use of animal alternatives in the National Toxicology Program?

Dr. Olden: The goals of the NTP in its current and future validation efforts are to develop, validate, and address the deficiencies of previously evaluated methodologies and to choose methods that can reduce our dependence upon the use of animals. Specific projects utilize computer-assisted chemical analysis and the latest methods of gene manipulation to develop non-animal models. There are two other systems that we are examining, the frog embryo and drosophila, or fruit flies, teratogenesis assays, to determine their usefulness in predicting the developmental, reproductive and neurotoxicity of environmental/industrial chemicals. Further, at the April NTP review, the NTP Board of Scientific Counselors will make recommendations on how to develop and validate better assays that may reduce the need for long-term testing in animals.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

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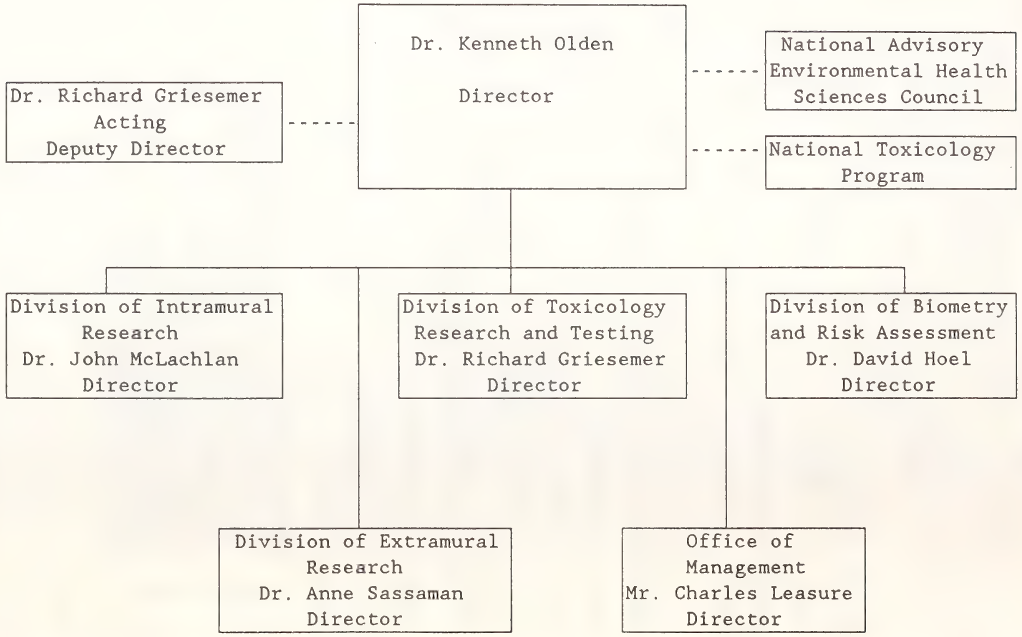
NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Organization Structure



NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

For carrying out section 301 and title IV of the Public Health Service Act with respect to environmental health sciences, [$253,902,000] $261,513,000: Provided, That of the funds made available under this heading, [$8,846,000] $12,304,000 shall not become available for obligation until September 30, [1992] 1993.

(Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 1992.)

NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Amounts Available for Obligation 1/

	1991 Actual	1992 Appropriation	1993 Estimate
Appropriation..................	$249,092,000	$253,902,000	$261,513,000
Sequester Order................	-3,000	---	---
Section 514(a) reduction.......	-2,061,000	---	---
Section 514(b) reduction.......	-6,003,000	---	---
Section 214 travel reduction...	---	-100,000	---
Section 513(a) travel reduction	---	-162,000	---
Section 513(b) S&E reduction...	---	-4,609,000	---
Subtotal, adjusted appropriation............	241,025,000	249,031,000	261,513,000
Real transfer from: NCI for cancer research.....	---	+3,000,000	---
Real transfer to other accounts for Shannon awards	-390,000	---	---
Subtotal, adjusted budget authority........	240,635,000	252,031,000	261,513,000
Unobligated balance, lapsing....................	-29,000	---	---
Total, obligations........	240,606,000	252,031,000	261,513,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1991 - $45,284,000; 1992 - $44,708,000; 1993 - $44,887,000.

Note: Excludes $15,000 for Royalties received in 1991.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Budget Mechanism
(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
Research Grants	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	268	$53,163	274	$56,223	290	$61,355
Administrative supplementals	(12)	480	(10)	468	(10)	484
Competing:						
Renewal	38	7,955	45	9,951	42	9,720
New	63	11,172	81	15,352	81	15,962
Supplementals	2	59	3	155	2	100
Subtotal, competing	103	19,186	129	25,458	125	25,782
Subtotal, research projects	371	72,829	403	82,149	415	87,621
Research Centers	17	16,673	17	16,934	17	16,934
Other Research:						
Research career programs	22	1,910	30	2,258	30	2,258
Minority biomed. res. support	--	488	--	462	--	462
Other research related	34	1,192	17	522	17	522
Subtotal, other research	56	3,590	47	3,242	47	3,242
Total, Research Grants	444	93,092	467	102,325	479	107,797
Training						
Individual awards:						
Noncompeting	23	654	30	843	21	593
Competing:						
New	27	654	8	152	17	402
Supplementals		--				
Subtotal, individ	50	1,308	38	995	38	995

Institutional awards:						
Noncompeting	488	9,243	410	9,753	410	9,755
Competing:						
Renewal	8	195	6	144	6	142
New	1	14	1	14	1	14
Supplementals	9	146	--	--	--	--
Subtotal, inst	506	9,598	417	9,911	417	9,911
Total, training	556	10,906	455	10,906	455	10,906
Research & Development Contracts	137	60,519	138	59,814	138	59,814
	FTEs		FTEs		FTEs	
Intramural Research	615	67,922	624	69,744	624	73,301
Research Management and Support	86	8,196	90	9,242	90	9,695
Total, NIEHS	701	240,635	714	252,031	714	261,513

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

CROSSWALK - 1991 Actual

(Dollars in thousands)

	MECHANISM								
	Research Grants			Training Programs		Research and Development Contracts	Intramural Research	Research Management and Support	Total
PROGRAM ACTIVITY	Research Projects	Research Centers	Other Research	Individual	Institutional				
Biological response to environmental agents................	$61,628		$3,590						$65,218
Applied toxicological research and testing..	5,289					$54,796			60,085
Biometry and risk estimation............	5,912					5,723			11,635
Resource and manpower development...........		$16,673		$1,308	$9,598				27,579
Intramural research.....							$67,922		67,922
Research management and support...........								$8,196	8,196
Total........	72,829	16,673	3,590	1.308	9,598	60,519	67,922	8,196	240,635

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

CROSSWALK - 1992 Estimate

(Dollars in thousands)

	MECHANISM								
	Research Grants			Training Programs					
PROGRAM ACTIVITY	Research Projects	Research Centers	Other Research	Individual	Institutional	Research and Development Contracts	Intramural Research	Research Management and Support	Total
Biological response to environmental agents................	$69,723		$3,242						$72,965
Applied toxicological research and testing..	6,406					$54,158			60,564
Biometry and risk estimation............	6,020					5,656			11,676
Resource and manpower development...........		$16,934		$995	$9,911				27,840
Intramural research.....							$69,744		69,744
Research management and support...........								$9,242	9,242
Total........	82,149	16,934	3,242	995	9,911	59,814	69,744	9,242	252,031

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

CROSSWALK - 1993 Estimate

(Dollars in thousands)

	MECHANISM								
	Research Grants			Training Programs					
PROGRAM ACTIVITY	Research Projects	Research Centers	Other Research	Individual	Institutional	Research and Development Contracts	Intramural Research	Research Management and Support	Total
Biological response to environmental agents................	$74,369		$3,242						$77,611
Applied toxicological research and testing..	6,838					$54,158			60,996
Biometry and risk estimation...........	6,414					5,656			12,070
Resource and manpower development...........		$16,934		$995	$9,911				27,840
Intramural research.....							$73,301		73,301
Research management and support...........								$9,695	9,695
Total........	87,621	16,934	3,242	995	9,911	59,814	73,301	9,695	261,513

National Institute of Environmental Health Sciences

Summary of Changes

1992 Estimated budget authority	$252,031,000
1993 Estimated budget authority	261,513,000
Net change	+9,482,000

	1992 Current Estimate Base		Change from Base	
	(Pos.) FTEs	Budget Authority	(Pos.) FTEs	Budget Authority
Changes:				
A. Built-in:				
1. Annualization of 1992 pay increases		$36,660,000		$+392,000
2. Within grade increases		36,660,000		+304,000
3. One less day of pay		36,660,000		-140,000
4. 1993 pay increase				+1,073,000
5. Increased cost of centrally furnished services		2,510,000		+366,000
6. Increased cost of Service and Supply Fund		1,865,000		+69,000
7. Increased cost of laboratory supplies, materials, and other expenses		37,951,000		+1,403,000
8. DHHS Working Capital Fund		287,000		+15,000
Subtotal				+3,482,000
	No.	Amount	No.	Amount
B. Program:				
1. Research projects grants:				
a. Noncompeting	274	56,691,000	+16	+5,148,000
b. Competing	129	25,458,000	-4	+324,000
Total	403	82,149,000	+12	+5,472,000
	Pos. (FTEs)		Pos. (FTEs)	
2. Intramural research	624	69,744,000	--	+496,000
3. Research management and support	90	9,242,000	--	+32,000
Subtotal, program				+6,000,000
Total changes				+9,482,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Budget Authority by Activity
(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	FTEs	Amount	FTEs	Amount	FTEs	Amount
Biological response to environmental agents...........	--	$65,217	--	$72,965	--	$77,611
Applied toxicological research and testing..........	--	60,085	--	60,564	--	60,996
Biometry and risk estimation........	--	11,635	--	11,676	--	12,070
Resource and manpower development.............	--	27,578	--	27,840	--	27,840
Intramural research.	615	67,903	624	69,744	624	73,301
Research management and support......	86	8,188	90	9,242	90	9,695
Total obligations...	701	240,606	714	252,031	714	261,513
Unobligated balance lapsing..........	--	29	--	--	--	--
Total Budget Authority........	701	240,635	714	252,031	714	261,513
HIV/AIDS............	(7)	(4,516)	(8)	(4,320)	(8)	(4,468)

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Budget Authority by Object

	1992 Appropriation	1993 Estimate	Increase or Decrease
Total number of full-time permanent positions................	546	546	---
Total compensable workyears:			
Full-time employment..............	762	763	+1
Full-time equivalent of overtime and holiday hours.........	4	4	---
Average ES salary....................	$103,900	$107,700	+$3,800
Average GM/GS grade..................	10.04	10.04	---
Average GM/GS salary	39,962	41,441	+1,479
Average salary, grades established by act of July 1, 1944 (42 U.S.C. 207)....................	62,639	64,957	+2,318
Average salary of ungraded positions.	26,670	27,657	+987
Personnel compensation:			
Full-time permanent	$21,486,000	$22,579,000	+$1,093,000
Other than full-time permanent.....	6,901,000	7,251,000	+350,000
Other personnel compensation.......	623,000	652,000	+29,000
Special personnel service payments.	1,984,000	2,077,000	+93,000
Total personnel compensation....	30,994,000	32,559,000	+1,565,000

	1992 Appropriation	1993 Estimate	Increase or Decrease
Personnel benefits	5,641,000	5,926,000	+285,000
Benefits for former personnel.....	25,000	25,000	---
Travel and transportation of persons....................	846,000	1,066,000	+220,000
Transportation of things..........	86,000	90,000	+4,000
Rent, communications, and utilities..................	6,883,000	7,227,000	+344,000
Printing and reproduction.........	304,000	319,000	+15,000
Other services:			
Project contracts...............	59,814,000	59,814,000	---
Centrally furnished services....	2,199,000	2,545,000	+346,000
Standard level user's charge....	311,000	331,000	+20,000
Other...........................	17,816,000	18,332,000	+516,000
Supplies and materials............	8,451,000	8,874,000	+423,000
Equipment.........................	5,430,000	5,702,000	+272,000
Grants, subsidies & contributions.	113,231,000	118,703,000	+5,472,000
Interest..........................	---	---	---
Total budget authority by object...............	252,031,000	261,513,000	+9,482,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Significant Items in the House, Senate and Conference Appropriations Committee Reports

National Toxicology Program

The Senate in its report 102-104, page 123 stated "The key problem in implementing new alternative methods is insufficient validation for effectiveness in large-scale, multilaboratory studies. The Federal Government's focal point for validating new tests is the National Toxicology Program (NTP), an interagency program specializing in toxicity testing. Unfortunately, the NTP's validation budget has not kept pace with inflation. Therefore, the Committee urges that an additional $1,000,000 be made available for the NTP's validation budget."

Action Taken or to be Taken - The increased funding will provide for the support of studies to validate methods of testing for environmental substances that cause birth defects, using insect and amphibian models.

Volcanic Emissions

The Conferees in their report 102-282, page 27, stated "The Conferees urge the Institute to explore the public health hazards associated with volcanic emissions on the Big Island of Hawaii."

Action Taken or to be Taken - Senior staff of the NIEHS have visited the University of Hawaii to consult with faculty of the School of Public Health. A second meeting is scheduled at NIEHS on January 27-28, 1992 and will include specific discussions of the public health hazards associated with volcanic emissions.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1992 Amount Authorized	1992 Appropriation	1993 Amount Authorized	1993 Budget Estimate
Research and Investigation.........	Section 301	42§241	Indefinite	$241,125,000	Indefinite	$250,607,000
National Institute of Environmental Health Sciences.............	Section 463	42§285	Indefinite		Indefinite	
National Research Service Awards........	Section 487(d)	42§288	Authorizing 1/ legislation is pending	10,906,000	Authorizing 1/ legislation is pending	10,906,000
Total Budget Authority				252,031,000		261,513,000

1/ This training authority is shared with other research training programs of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Appropriation History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1984	$165,884,000	$173,627,000 2/	$172,374,000 2/	$179,802,000
1985	183,755,000	189,437,000 3/	191,908,000	194,056,000
1986	183,755,000	188,319,000 4/	198,319,000	197,478,000
1986 Sequester				-8,492,000
1987	187,995,000	209,872,000	208,067,000	209,294,000
1988	198,431,000	225,724,000 5/	220,709,000	215,666,000
1989	218,471,000 6/	216,985,000 7/	223,168,000	223,454,000 8/
1990	226,471,000 9/	232,479,000	234,048,000	232,476,000 10/
1990 Sequester				-3,242
1991	235,792,000	244,832,000 11/	242,765,000	241,028,000 12/
1991 Sequester				-3,000
1992	254,484,000	254,912,000	250,873,000	249,031,000 13/
1993	261,513,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.

2/ Excludes $5,319,000 in NRSA training programs not considered.

3/ Excludes $5,922,000 in NRSA training programs not considered.

4/ Excludes $8,502,000 in NRSA training programs not considered.

5/ The House allowance consolidated AIDS funding ($4,091,000) in the Office of Assistant Secretary for Health.

6/ The 1989 request excludes funding for AIDS research and education ($4,234,000) proposed for consolidation in the Office of the Assistant Secretary for Health.

7/ Excludes $9,183,000 in NRSA training programs not considered.

8/ Excludes $2,714,000 administrative reduction.

9/ The 1990 request excludes funds for the National HIV program ($4,377,000) proposed for consolidation in the Office of the Assistant Secretary for Health.

10/ Excludes $788,000 enacted administrative reduction.

11/ Excludes $10,586,000 in NRSA training programs not considered.

12/ Excludes enacted administrative reduction of $8,064,000.

13/ Excludes enacted administrative reduction of $4,871,000.

Justification

National Institute of Environmental Health Sciences

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
701	$240,635,000	714	$252,031,000	714	$261,513,000	---	+$9,482,000

General Statement

The National Institute of Environmental Health Sciences (NIEHS) conducts and supports research on the health effects arising from exposures to the chemical, biological, and physical world in which we live. These exposures can exert their effects in two ways - they can be the direct cause of a disease, such as when asbestos exposure leads to development of the lung cancer, mesothelioma; or they can be a component of a disease state, such as when high ozone levels aggravate an existing asthma condition. Thus the spectrum of human diseases and dysfunction with potential environmental causes or components is very broad. Relevant conditions would include cancer, birth defects, infertility, immune disorders, neurological defects, asthma, and kidney disease.

The study of environmentally related diseases is a challenging one. It is significantly complicated by a number of factors, including the fact that most people are exposed to multiple environmental agents at widely varying dose levels; that many years can elapse between an exposure and the final development of a disease; that multiple organ systems can be affected; and that the exact form an environmentally caused disorder can take might vary depending upon the age and nutritional status of the individual at the time of exposure. Despite these many complicating factors, the study of environmental components of human disease and dysfunction is critical. Because of the wide range of potential environmentally-related diseases and because many of these exposures can be prevented or significantly reduced, determining the role of environmental factors in the broad spectrum of potential health disorders is obviously cost-effective. This information, used to design early prevention and intervention strategies, could circumvent the need for later, more costly, treatment of chronic or disabling diseases.

Defining environmental causes and components of human disease and dysfunction requires collaborative efforts between molecular biologists, toxicologists, epidemiologists, and physicians. It is the NIEHS mandate to bring together all these critical elements through a research program which balances the efforts of intramural staff scientists with extramural efforts conducted via grant support of university-based researchers and contracts for studies by private research institutions. Directing and coordinating these efforts requires that the Institute maintain open communication not only with its own Institute-supported scientists, but with other governmental organizations and the public at large. The training of scientists and medical professionals who provide the manpower for environmental health sciences research and environmental and occupational medical services are also supported.

The Institute conducts and supports both "applied" and "basic" research programs to gain an understanding of environmental components of human disease. In "applied" research programs, environmental agents - e.g., pharmaceuticals, radiation, pesticides - are studied either in animal surrogates or in already exposed human populations to determine the potential of a particular agent to cause adverse health effects. The "basic" research component examines the molecular and cellular basis of biological functions and the mechanisms by which environmental agents disrupt these functions. Neither of these approaches exists in isolation; rather they complement one another in furthering our understanding of the effects of environmental agents and ways in which these effects can be treated or mitigated. Recent NIEHS-supported research on lead illustrates the vital role both approaches can play.

Lead is a common environmental contaminant which adversely affects the central nervous system. Children, because their brains are still developing, are particularly vulnerable to adverse effects of lead. Additionally, although lead poisoning can occur at all socioeconomic levels, the urban poor seem to be primary victims. Prior to NIEHS-supported research on lead, blood lead levels of 25 μg/dL had been thought safe. However, it has recently been shown that levels as low as 7 - 10 μg/dL are associated with decreased intelligence and slower neurobehavioral development. Although these effects are subtle, they translate into a significantly higher likelihood of learning disabilities and school drop-out later in life. The results of this applied research project are in part responsible for increased efforts by HHS, EPA, and HUD to further reduce childhood lead exposures.

At the same time that the Institute was supporting the above applied research program, basic research projects into the mechanisms of lead toxicity were also being conducted. These studies showed that lead affects metabolism of several important nutrients, particularly vitamin D and calcium. These findings suggest that ensuring adequate nutrition affects lead burden in children which in turn might ameliorate the subtle neurobehavioral deficits associated with low lead exposures, a possibility further substantiated by epidemiological studies showing that poor nutritional status exacerbates the effect of lead in children. Thus a coordinated effort, including both applied and basic research into the toxicity of lead, has brought us to the point where we can design potential intervention strategies for children at risk from low levels of lead exposure.

Summary of Recent Accomplishments

The research programs conducted and supported by the Institute consistently produce new findings that broaden the understanding of the relationship between human health and the environment. Several examples include:

- development of a new drug, dihydrexidine, which can dramatically reduce neurological symptoms in primates in whom Parkinson's disease has been chemically induced. These laboratory studies hold promise in treating Parkinson's disease, as well as parkinsonism induced by environmental chemicals.

- studies which showed that 1,3-butadiene, a compound to which potentially 52,000 workers in the synthetic rubber industry are exposed, was a more potent carcinogen than originally thought. Based on the study results, the Occupational Health and Safety Administration is considering lowering the current allowable occupational exposures 500-fold.

- cloning of the human prostatic acid phosphatase (PAP) gene. The protein product of this gene is used in the diagnosis of prostate cancer. By being able to clone the gene, researchers will be better able to study how environmental factors can cause expression of this gene and how this gene expression relates to development and progression of prostate cancer.

Direction of Current Research

NIEHS is conducting research on many of the "headline" issues of concern to the average citizen. Clinical studies are being designed to determine if the mercury in dental amalgams causes any neurobehavioral deficits in children. Epidemiologic studies are underway which will help separate the health effects of household radon exposure from that of radon exposure in combination with cigarette smoking. Animal studies will be conducted which will begin to define the actual potential of electromagnetic fields to cause changes in biological organisms. These are but a few examples of the important applied research projects underway.

Equally important are the basic research projects being contemplated. For example, a class of chemical receptors, the so-called "orphan receptors", has been identified. Numerous environmental agents have been shown to bind to these receptors and, in some instances, to initiate critical cellular events. This information potentially could be crucial in finding an environmental component for a number of diseases and disorders. The Institute plans to investigate these "orphan receptors", to define their normal biological function, and to determine the biological consequence of these receptors high affinity for binding to environmental compounds. Research will also continue on the mechanism of action of dioxin toxicity, as mediated via the Ah receptor, to help in the debate over the current EPA limits on dioxin levels and whether higher levels would be equally safe.

Emerging Opportunities and Future Plans

The NIEHS recognizes the need to enhance the clinical component of environmental health studies. This past year, a Director of Clinical Research was named. His office is responsible for translating promising laboratory findings into practical applications for human needs. Regular review of environmental health science research conducted and supported by the Institute should lead to early identification of study results which could be used experimentally in a clinical setting to treat people suffering from environmental exposures. Among the clinical studies being considered are evaluations of the potential of nutritional interventions for reducing lead toxicity in exposed children, evaluation of lead chelating agents which would remove lead from the bodies of exposed people, and determination of environmental components of chronic lung diseases.

Environmental equity is a new topic of research interest for NIEHS. It refers to the differential potential environmental risks people face depending upon where they choose to live. Some expect that the poor are at greater risk of environmentally-related diseases than are middle and upper-income earners. To date, scientific information has not been collected to refute or validate the existence of such potential environmental equity problems. NIEHS plans to develop the type of scientific database that could be used to provide answers to this and other questions involved in environmental equity.

Purpose and Method of Operation

The purpose of NIEHS' research is to identify and characterize chemical and physical environmental agents that threaten human health and to study the means by which environmental agents cause illnesses. This purpose is accomplished through Federal funding of direct intramural research and support and various extramural mechanisms.

The investigator-initiated research project grant program is the Institute's primary mechanism for supporting studies conducted by university scientists. These studies involve programs related to biological response to environmental agents, applied toxicological research and testing, and biometry and risk estimation. The scientists use all available tools of biomedical research, including basic biomedical studies, epidemiology, and toxicology. For the most part, this mechanism supports either a discrete, specified project by the named investigator or a broadly based, multidisciplinary program that includes several projects that have a specific major objective or basic theme. NIEHS continues to encourage the use of research grant supplements designated to provide minority undergraduate, graduate and postdoctoral students and to minority faculty with environmental health science experience by training these students in the techniques and theory on which the grants are based.

Through grants to research Centers it is possible to assemble a critical mass of scientific talent and apply it to the complex scientific questions which typify all environmental health problems. The centers are a national resource for responding to environmental health research needs from the local to the international level. Supplemental funds are available to the centers for data collection and evaluation in the event of major accidents or disasters. In addition, the centers can support small pilot projects that enable a researcher to determine if a comprehensive research grant application is feasible.

Through the research career program, the Institute promotes and supports career development of researchers by issuing research career development awards, academic/teacher awards, clinical investigator awards, and physician scientist awards. This mechanism supports the Environmental/Occupational Medicine Academic awards initiated in FY 1991.

Other research grant awards support major conferences, small instrumentation, and scientific review and evaluation activity.

The National Research Service Award program supports research training of scientists for careers in basic and applied research into the human health implications of environmental exposures. The training is concentrated in the areas of toxicology, pathology, reproductive biology, mutagenesis, epidemiology and biostatistics, and molecular biology. Fellowship awards are made to individuals and training grants are made to institutions. The goal is to supply the critical scientific expertise necessary to solve environmental health problems encountered by individuals, patients, and the community in which they reside. It is also the goal of this program to reach out to underutilized populations, such as minorities and women, and encourage their participation as members of the environmental health sciences workforce.

The research and development contract mechanism is used to support specific research studies characterizing chemical toxicity and improving the testing methods used to determine toxicity and to support studies in basic and applied statistics, biomathematics, epidemiology, molecular modeling, and risk assessment.

The intramural research activity is made up of three major scientific divisions plus associated technical and administrative support. The Division of Intramural Research concentrates on understanding the mechanisms by which the environment alters the body's normal functions; the Division of Toxicology Research and Testing studies chemicals that pose potential hazards to humans and develops relevant methodology to establish easier, less costly ways to determine toxicity of various types; the Division of Biometry and Risk Assessment plans and conducts research in quantitative and biochemical risk estimation, statistics, biomathematics, and epidemiology.

The research management and support activity provides salary and other support for the Office of the Institute Director, the Division of Extramural Research and Training, and portions of the Office of Management.

Funding for the NIEHS during the last 5 years has been as follows:

	Amount	FTE
FY 1988	$211,763,000	689
FY 1989	223,686,000	667
FY 1990	228,739,000	667
FY 1991	240,635,000	701
FY 1992	252,031,000	714

Overall Budget Policy

The FY 1993 budget request for NIEHS is $261,513,000, an increase of $9,482,000 over the FY 1992 estimate. Sixty-eight percent of the budget request would support research grants, training, and contract activities, and 32 percent of the request would support intramural research and research management activities. AIDS-related research funds of $4,468,000 are included.

In FY 1993, the budget request would fund 125 competing research project grants at an average cost of $206,300. The average cost is 4.5 percent greater than the FY 1992 estimate. The anticipated success rate in the budget request is 30 percent. The FY 1993 budget request would support 290 noncompeting research project grants at an average cost of $211,600. The average cost of noncompeting grants is 3.1 percent more than in FY 1992.

Twelve environmental health sciences centers and five marine and freshwater biomedical sciences centers would receive $16,934,000 in support from this request and other research grants would receive $3,242,000.

The 1993 request would support 455 research trainees at an estimated cost of $10,906,000.

Contracts to support research and development in toxicity testing and test development, in risk estimation methods, and for other scientific problems in environmental health are projected at $59,814,000. Approximately 138 contracts would be supported.

Intramural research funds of $73,301,000 and 624 FTEs and research management and support funds of $9,695,000 and 90 FTEs are requested.

National Institute of Environmental Health Sciences

Biological Response to Environmental Agents

Authorizing Legislation - Section 301 and 463 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$65,218,000	$72,965,000	$77,611,000	+$ 4,646,000

Detecting the more subtle impact of environmental agents on human health and developing an ability to predict outcomes at low levels of exposure requires strengthening the mechanistic basis of hazard identification. This strategy involves a detailed understanding of how environmental agents act at the most fundamental levels of biological organization - the genes and proteins controlling all function and communication - to disrupt normal processes, leading to human disease or dysfunction. By understanding how environmental agents exert their effects at the cellular and molecular levels, scientists can better devise strategies to circumvent or prevent these effects.

Funding for the Biological Response to Environmental Agents activity during the last 5 years has been as follows:

	Amount
FY 1988	$54,097,000
FY 1989	58,068,000
FY 1990	60,410,000
FY 1991	65,218,000
FY 1992	72,965,000

Rationale for the Budget Request

The FY 1993 budget request for Biological Response to Environmental Agents is $77,611,000, a 6.4 percent increase over the FY 1992 estimate of $72,965,000.

Human exposures to environmental agents occur, literally, from conception to death. Every organ system is potentially a target for the action of environmental agents. The NIEHS supports research which covers this broad range of potential biological responses to the environment. Two critical systems, the developmental system and the immune system, illustrate the type of research supported.

Early Fetal Development

Environmental Factors Leading to Implantation Failure and Spontaneous Abortion: Environmental factors may contribute significantly either to failure of a fertilized egg to implant in the mother's womb or to the occurrence of spontaneous abortions in women wanting to become pregnant. Two environmental compounds, mercury and cadmium, have been shown to adversely affect biological events critical to early fetal development. Mercury is known to cause breakdown of the basement membrane in exposed tissue; a by-product of that destruction is the release of a protein called laminin. The body's immune system produces antibodies against this protein and the individuals develop an autoimmunity. Because of this autoimmunity, the antibodies produced react against the fertilized egg, prevent implantation, and result in reproductive failure. Nonetheless, the developing embryo does have certain defense mechanisms for responding to some degree of toxic insult. NIEHS-supported researchers have been looking at the expression of metallothionein genes in the embryo and reproductive tract. The products from these genes are instrumental in protecting the embryo from toxic metals such as cadmium, which can have dramatic effects on early fetal development. These genes are able to produce proteins which bind to heavy metals, preventing them from interacting with the fetus and disrupting its early development. These same researchers have developed strains of transgenic mice, providing an animal model for studying the critical regulatory pathways which can be disrupted by environmental agents. Information from this research could potentially lead to important preventive measures to help women carry their children to full-term.

Birth Defects: Birth defects continue to be a major concern to the NIEHS. One out of 33 live births results in a child with a birth defect and 70% of these human birth defects have an unknown cause. One class of ubiquitous environmental and occupational pollutants, N-nitroso compounds, has been shown to cause birth defects. These agents are toxic to several target organ systems, but the developing nervous system is especially sensitive. NIEHS-funded scientists are developing biomarkers for central nervous system differentiation which may prove useful in detecting neuron-specific toxicity. In addition, this laboratory is studying the effects of growth factors in embryo culture systems. Preliminary evidence suggests that a naturally occurring protein, transforming growth factor beta, may be able to reverse the poor cell growth effects brought on by exposure to N-nitroso toxicants. Such a protective role for this growth factor might have important implications for improving public health safety following toxic exposures.

Immune System Effects

There is increasing awareness that environmental agents can cause subtle changes in immune system processes and, thus, increase the frequency or severity of immunologically controlled diseases such as infections and cancer. For example, UV radiation is a known immunosuppressant. NIEHS-supported research has demonstrated that chronic exposure to UV radiation significantly shortens the life span of laboratory animals. The possibility that immunosuppression plays a key role in this finding needs to be explored, particularly since thinning of the ozone layer will result in increased human exposure to UV radiation. Other common environmental agents which adversely affect the immune system include lead, dioxin, benzene, nickel sulfate, and dimethylnitrosamine. Thus, there is a continued need to identify the effects of environmental compounds on the immune system and to define their impact on human health.

Because of these research needs in immunotoxicology, the NIEHS, in conjunction with the National Institute of Allergy and Infectious Diseases (NIAID), has issued a program announcement to foster "Studies on the Interactions between Environmental Toxicants and the Immune System." The interest in environmental immunotoxicants is focused on three broad research categories: suppression/inhibition of immunological competence; initiation or triggering of autoimmunity; and stimulation of allergic/hypersensitivity reactions. The first area of research will be the major focus for the NIEHS whereas the last area is predominantly NIAID. Both Institutes place emphasis on research studying the initiation of autoimmunity.

National Institute of Environmental Health Science

Applied Toxicological Research and Testing

Authorizing Legislation - Section 301 and 463 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$60,085,000	$60,564,000	$60,996,000	+$ 432,000

This activity supports studies characterizing chemical toxicity and improving the testing methods used to determine toxicity. The Institute mission in these efforts is to expand our knowledge of the health effects of environmental agents. NIEHS scientists develop research protocols for the development, evaluation, and validation of test methods and procedures. These protocols are used by contract laboratories to conduct studies under the management of NIEHS scientific staff. Data from these studies are reported and used to protect public health and prevent diseases linked to environmental exposures.

Funding for the Applied Toxicological Research and Testing activity during the last 5 years has been as follows:

	Amount
FY 1988	$57,675,000
FY 1989	61,070,000
FY 1990	56,590,000
FY 1991	60,085,000
FY 1992	60,564,000

Rationale for the Budget Request

The FY 1993 budget request for this activity is $60,996,000, an increase of 1.0 percent over the FY 1992 estimate of $60,564,000. The following are examples of research efforts funded in this budget activity.

National Toxicology Program

NIEHS provides the largest component of the National Toxicology Program (NTP), the intragovernmental cooperative program for testing chemicals that may affect human health. Environmental agents are nominated for NTP testing by public and private sources, including federal, local and state agencies; unions; industry; academia; and members of the general public. The nominations are evaluated by a panel of experts from Federal research and regulatory agencies.

Cancer Studies

NIEHS efforts under the NTP continue to identify critical hazards in our environment. Recently the common paint stripper and degreasing agent, 1,2,3-trichloropropane, was shown to have clear cancer-inducing properties based on rodent studies. This fact is important because, not only is 1,2,3-trichloropropane used both in household and industrial settings, it has been found in groundwater in a number of states. Another compound with wide exposure, naphthalene, was tested. This chemical is used in moth balls and was found to exhibit some evidence of carcinogenicity in female mice, although it was not carcinogenic in male mice.

In the area of occupational exposures, a compound used in the synthetic rubber industry, 1,3-butadiene, was found to be clearly carcinogenic in mice. Based on the NTP study results, the Occupational Safety and Health Administration is proposing that the current occupational standard be reduced 500-fold, from 1000 ppm to 2 ppm. Since approximately 52,000 workers are potentially exposed to this chemical, lowering their exposure could have long-term benefits in terms of improved health and longevity.

Electromagnetic Fields (EMF)

Recent epidemiologic studies suggest that low-frequency electromagnetic fields, of the sort emitted by power lines and electrical appliances, might cause cancer in adults and children. Given the large exposures to these fields, it is imperative that a well-designed study be conducted to assess the effects of these fields on biological systems. The NIEHS assembled a team of experts, including scientists from the electrical power industry, that designed studies which can best answer these questions.

Non-Cancer Endpoints

Although cancer remains the endpoint for which NTP is most identified, it is actually only one of the many health effects evaluated by the Program. Important studies are also conducted to determine the effect of chemicals on other organ systems, including the nervous system, immune system, and reproductive system. For example, it was recently found that boric acid, a chemical commonly used to kill cockroaches, is toxic to the male reproductive system. This study result is important because this compound is readily available to the consumer, who might not use the proper safety precautions when using boric acid around the home to control cockroaches.

Validation

The NTP also continues to validate new toxicity assays and to evaluate alternative animal test methods and assays for hazard identification. Toward this end, a workshop was held in November 1991 to assess the value of fish in assessing the cancer-causing ability of chemicals. Other work is ongoing to evaluate the use of the folliculogenesis assay, in which the number of follicles in the female reproductive tract are counted following exposure to suspected reproductive toxicants, as a method to help define the actual target of the action of a reproductive toxicant. If the value of this assay can be established, it will enable reproductive toxicologists to extract more information from the same study and would reduce the need for additional animals to explore the site of action of a reproductive toxicant.

AIDS

The Institute continues to serve as a national resource for testing of the side-effects of AIDS therapeutics and of combinations of these therapeutics. As an increasing number of AIDS victims are pregnant women, the Institute's research into the effects of these therapeutics on the developing fetus will play an increasingly significant role in helping physicians designing treatment strategies that help the mother with minimal adverse effects on her developing child. Already studies have shown that a proposed drug, ddC, causes some skeletal deformities in rodents when the fetus is exposed to very high doses. This information can be used in setting safe dose regimes for human use.

National Institute of Environmental Health Science

Biometry and Risk Assessment

Authorizing Legislation - Section 301 and 463 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$11,635,000	$11,676,000	$12,070,000	+$ 394,000

Important elements of this research include qualitative and quantitative estimates of the adverse health effects of exposure to environmental agents, and the development of experimental and computer-based models that may be useful in identifying environmental risk factors and the biological mechanisms involved.

Funding for the Biometry and Risk Assessment activity during the last 5 years has been as follows:

	Amount
FY 1988	$8,295,000
FY 1989	9,631,000
FY 1990	11,692,000
FY 1991	11,635,000
FY 1992	11,676,000

Rationale for the Budget Request

The FY 1993 budget request for this activity is $12,070,000, an increase of 3.4 percent over the FY 1992 estimate of $11,676,000. The following are some examples of research supported by this budget activity.

Biomarkers

Assessing the risk associated with specific exposures is often made difficult by the lack of quantitative exposure data for individuals within exposed populations. Monitoring data and/or estimates constructed by modeling often represent the only exposure information available, and therefore, average population exposure is the sole parameter for use in studies of health effects. This process is obviously less precise in estimating health outcomes than using specific markers of individual exposure (and doses) in human effects studies. The NIEHS gives high priority to developing these "biomarkers" because they could be used both to define individual risks, exposures, and diseases, and to improve the methodology used by epidemiologists and risk assessors.

4-Aminobiphenyl Adducts: Biomarkers can be developed in cases where environmental chemicals bind to body proteins (so called "adduct" formation) which are often easily collected and assayed, such as hemoglobin in blood. Research on adduct formation between hemoglobin and the common carcinogen in tobacco smoke, 4-aminobiphenyl, has yielded important information. Studies during the past year have revealed that levels of hemoglobin adducts of 4-aminobiphenyl accurately and quantitatively reflect exposure in both smokers and non-smokers. Adduct levels also decline in a predictable manner upon cessation of smoking. Importantly, in studies of smokers of different tobacco types, adduct levels clearly reflected an individual's ability to metabolize this compound and this ability correlated with elevated risk of bladder cancer. In other words, the stronger the tobacco, the higher the adduct levels, and the higher the risk of urinary cancer. Most recently, studies of newborn infants of smoking and non-smoking mothers revealed the presence of 4-aminobiphenyl adducts in hemoglobin of the infants at levels reflective of the exposure history of the mothers. Thus, this approach provides a sensitive and accurate means of monitoring prenatal exposure to maternal smoking metabolites and demonstrates the technique's potential to monitor exposures to a wide variety of carcinogens.

Acrylamide Adducts: It is important to determine whether individuals exposed to toxic chemicals at low levels for prolonged periods of time can be identified by measuring derivatives from these toxic molecules on their hemoglobin. Since hemoglobin is not degraded rapidly, and has a long lifetime in the body, it is possible to detect the accumulation of adducts on this protein molecule even when exposures occur over a prolonged period of time. To investigate whether hemoglobin adducts provide a reliable estimate of the internal dose to toxic compounds, acrylamide was chosen because of its ability to react directly with proteins and its substantial neurotoxic potential. Acrylamide is used widely in the biomedical field, but its greatest use is as a polymerization agent in a variety of industrial processes. Within the past year, NIEHS-supported scientists have developed a high performance liquid chromatography system which detects two adducts resulting from the reaction of acrylamide with blood serum. However, they also found that acrylamide reacts somewhat differently with the nervous system proteins, the neurofilament, leading to the formation of a chemically distinct adduct. The ability to detect acrylamide adducts on blood proteins might serve as an index of exposure, and as such, might have predictive value in assessing the extent of damage to the nervous system, even though the structure of the adduct in the nervous system is chemically different. Similar studies are also being done on the neurotoxicant, n-hexane, a common solvent used in a variety of chemical processes and a component of gasoline.

Grain Dust and Lung Disease

More than 300,000 U.S. workers are exposed to grain dust and about 30 percent of them develop symptoms of bronchitis. NIEHS is supporting epidemiological studies of the relationship between exposure to mixed grain dust and development of lung disease. The goal is to understand the development of grain dust-linked lung disease in order to develop prevention and treatment plans. These studies may also contribute to understanding other respiratory ailments, including asthma. New information on preventing and treating asthma could be especially helpful for young African-American males, among whom the incidence of asthma is three to seven times that for Caucasian-American males.

National Institute of Environmental Health Sciences

Research and Manpower Development

Authorizing Legislation - Section 301, 463, and 487 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$27,579,000	$27,840,000	$27,840,000	---

The National Institute of Environmental Health Sciences supports the development of key national resources in environmental public health and the training of environmental health scientists through three major grant programs: Environmental Health Sciences Core Centers, Marine and Freshwater Biomedical Sciences Centers, and National Research Service Awards grants.

Funding for the Resource and Manpower Development activity during the last 5 years has been as follows:

	Amount
FY 1988	$25,255,000
FY 1989	25,271,000
FY 1990	27,136,000
FY 1991	27,579,000
FY 1992	27,840,000

Rationale for the Budget Request

The FY 1993 budget request for this activity is $27,840,000, the same as the FY 1992 estimate. The following are examples of efforts supported by this budget activity.

Research Centers

The Centers program supports institutions with existing research programs in environmental health by funding core resources and administrative structure for these efforts. The purpose is to better focus research efforts on issues relating to the mission of the Institute, to provide a productive environment for these efforts, and to provide some stability and means for program enhancement and growth of the field. In addition, the centers are sources of expertise to NIEHS for evaluation of environmental incidents or for problem evaluation. A center grant provides support for core facilities and associated technical staffs and administrative structure to stimulate interdisciplinary studies on the health effects of human environmental exposures. Funds are also provided for pilot project efforts, enrichment activities such as seminars and visiting scientists, and for center development, including new investigator support.

New center program guidelines were issued in FY 1991 to clarify the nature of support provided by such a grant. Center directors and new applicants are using these guidelines to streamline and organize their research programs to make more effective use of the support provided. An important result of the new structure will be that a center will be a distinct entity within an institution's organizational structure, ensuring optimal management and administration by both the institutional director and NIEHS staff.

The current center program is comprised of twelve large core center grants and five Marine and Freshwater Biomedical Science Centers. Important findings arising from center-supported research include:

- development of a new vibrotactile technique for assessing environmental nerve damage. This technique can replace electrophysiological measurements in field settings and has now been tested in a group of pesticide applicators in Central America.

- studies of skin cells exposed to sunlight which led to identification of a reactive oxygen species capable of damaging DNA. Using state-of-the-art fluorescence cell counting, hydrogen peroxide was demonstrated to be present in exposed skin. Hydrogen peroxide was also found in the skin of animals treated with a potent tumor promoter and in malignant melanoma cells subject to UV light, findings which are highly pertinent to understanding causes of human cancer.

- identification of specific enzymes responsible for converting aflatoxin, a compound excreted by molds growing on corn and peanuts, into a form which causes liver cancer. This information is useful in determining the exact reaction pathway to the DNA adducts thought to initiate the tumors. In related research, another center investigator has found that the antioxidant, oltipraz, can prevent the aflatoxin-induced liver cancer in laboratory animals. These results can have important implications in designing therapeutic interventions for populations living in areas with high incidences of liver cancer thought to be related to aflatoxin exposure.

- determination that exposure to ozone during normal outdoor exercise can produce marked decreases in respiratory function in otherwise healthy adults. These affects are greater in outdoor studies than in controlled indoor chamber studies, indicating that the adverse effects of ozone are probably enhanced by simultaneous exposures to other common air pollutants.

Research Training

The Institute's research training is concentrated in the areas of toxicology, pathology. reproductive biology, mutagenesis, epidemiology and biostatistics, and molecular biology. A major thrust of this program is to reach out to under-utilized populations, such as minorities and women, and encourage their participation as members of the environmental health sciences workforce.

National Institute of Environmental Health Sciences

Intramural Research

Authorizing Legislation - Section 301 and 463 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
615	$67,922,000	624	$69,744,000	624	$73,301,000	---	+$3,557,000

Institute scientists provide a critical link between basic and applied environmental research. The close proximity of individual laboratories offer many opportunities for sharing ideas and research findings. Thus, NIEHS intramural scientists involved in research on cellular and molecular processes can interact with intramural scientists doing applied research and, together, they can develop a more mechanistic understanding of environmental health problems.

Funding for the Intramural Research program during the last 5 years has been as follows:

	Amount	FTE
FY 1988	9,446,000	605
FY 1989	62,157,000	581
FY 1990	64,809,000	583
FY 1991	67,922,000	615
FY 1992	69,744,000	624

Rationale for the Budget Request

The FY 1993 budget request for Intramural Research is $73,301,000, an increase of 5.1 percent over the FY 1992 estimate of $69,744,000. The following are examples of efforts supported by this budget activity.

Dioxin

Dioxin is an environmental contaminant which has been the subject of revived regulatory interest. It is formed in the paper-making process when chlorine is used to bleach wood pulp. Dioxin is then released into nearby streams, becoming concentrated in the tissues of fish and other aquatic animals. Because dioxin is a known human carcinogen, EPA regulates the amounts allowed for human consumption. The current standard for dioxin levels in drinking water is 13 parts per quintillion.

Epidemiologic studies have presented conflicting evidence about the relative potency of dioxin's cancer-inducing properties. Some studies suggest that it is a potent carcinogen; others, that the carcinogenicity might be less than currently thought. These results have led to industry demands that EPA re-evaluate its dioxin standard and consider raising the limit. It is in this arena of public health policy that NIEHS' long history of dioxin-related research is proving fruitful.

Institute scientists have developed a detailed understanding of the dioxin protein receptor (called the Ah receptor). Binding of dioxin to this receptor is the critical biological event for all subsequent aspects of dioxin toxicity. Our research has addressed the controversial issue of dose response relationships, upon which industry is basing its claims that the dioxin standard is currently too stringent. Because dioxin toxicity relies upon binding to a receptor, some scientists claim that this means that there is a "threshold" for toxicity - that is, the body can tolerate a certain amount of dioxin until a critical number of receptors has been bound to molecules of dioxin. If true, this might mean that the EPA standard, which was based on a no-threshold, linear dose-response concept, would be too conservative and could be safely raised. NIEHS scientists designed experiments to determine if dioxin's effects exhibit a threshold effect. This work has disproved the claim that receptor-mediated toxicities imply the presence of a threshold. Other aspects of the work have demonstrated that animal models are appropriate for estimating human risks and that there is considerable inter-individual variation in human response to dioxin and that this fact complicates the risk assessment process. Researchers are now working to determine the mechanistic link between biochemical/molecular changes and toxicity so that uncertainty in EPA's risk assessment process can be minimized. In these ways, NIEHS serves as an impartial source for environmental health studies which can be used in the more politically charged arena of public regulatory policy.

Orphan Receptors

Another class of protein receptors, the so-called "orphan receptors", suggest exciting avenues of research for exploration. These receptors have a high affinity for binding to certain classes of environmental compounds and, in some cases, this binding has been shown to initiate biological events. The full biological role of these receptors has yet to be elucidated but, when these roles have been defined, they will probably give us new clues into how environmental agents interact with these receptors to disrupt normal cell growth, differentiation, and development. Knowledge gained from these studies will suggest new roles for environmental compounds in the etiology of human disease and dysfunction.

Environmental Estrogens

NIEHS scientists continue to be among the world leaders in the study of how environmental estrogens affect development and health. Research has shown that estrogenic environmental agents can disrupt reproduction and increase cancer risk. These hormone-like substances can also influence metabolism and cardiovascular health. For these reasons, intramural scientists are continuing to investigate the role of these compounds in human health and hope to extend their laboratory findings into a more clinical setting.

Molecular Modeling

Institute scientists are also attempting to harness emerging computer technologies to enhance our ability to use computer imaging to predict probable chemical interactions with genes and proteins. By developing the ability to project molecular models onto a video display terminal, scientists can visualize, in two and three dimensions, the structure of the molecule and manipulate these structures to see how vulnerable they are to alteration by environmental chemicals. This work will greatly accelerate our ability to develop a mechanistic understanding of how environmental agents affect biological systems. This technology is potentially very powerful and could be useful in risk assessment, in reducing the need for animals in toxicity testing, and in designing pharmaceuticals and pesticides which have maximum effectiveness with minimal side effects.

National Institute of Environmental Health Science

Research Management and Support

Authorizing Legislation - Section 301 and 463 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
86	$8,196,000	90	$9,242,000	90	$9,695,000	---	+$ 453,000

Responsibilities covered by this budget category include directing, coordinating, and evaluating Institute-wide programs and policies, and reviewing and administering grants, contracts, and cooperative agreements.

Funding for the Research Management and Support program during the last 5 years has been as follows:

	Amount	FTE
FY 1988	$6,995,000	84
FY 1989	7,489,000	86
FY 1990	8,103,000	84
FY 1991	8,196,000	86
FY 1992	9,242,000	90

Rationale for the Budget Request

The FY 1993 budget request for research management and support is $9,695,000, an increase of 4.9 percent over the FY 1992 budget estimate.

Research Management and Support provides salary and other support for the immediate Office of the Institute Director, the Division of Extramural Research and Training, and portions of the Office of Management, including central financial and personnel management, and the Institute's information office.

National Toxicology Program

Support for administrative functions of the National Toxicology Program is included in this activity. The Institute Director is also the Director of the NTP and is responsible for coordinating the NTP-related programs of NIEHS and other Federal agencies that take part in programs to identify and characterize the effect of environmental agents that may adversely affect human health. In FY 1992 the NIEHS, along with other NTP agencies, plans to convene a panel of experts to review the program to ensure that it is optimally:

- selecting chemicals with greatest public health significance for study;
- adequately addressing issues of mechanisms of action, as well as hazard identification;
- developing and validating assays which will reduce the need for long-term testing in animals; and
- alerting regulatory agencies and the public about test results on important chemicals.

The above efforts are part of an ongoing process to guarantee that high priority research needs are being addressed and that this research is of the highest quality possible.

Task Force IV

The National Advisory Environmental Health Sciences Council convened a Task Force to prepare a report on research needs and opportunities in the area of environmental health. This is the fourth Task Force on environmental health research; it encompasses a review of the broad concerns within environmental health research and how emerging technologies and cellular and molecular techniques can be used to creatively address these concerns. Recommendations from Task Force IV, due in final form January 1992, will directly affect research policies and directions for both the intramural activities and the extramural programs it supports.

Strategic Plan

NIEHS was also an active player in development of the NIH strategic plan. Environmental health issues were identified in almost all of the fifteen areas of scientific opportunity. In addition the area of "Basic Biology and the Environment", for which NIEHS had the lead role, served to map an NIH-wide research policy for how advances in cellular and molecular biology will be coupled with defining how environmental interactions with critical genes and proteins can lead to human disease and dysfunction.

Facilities

The Institute will continue to review and update plans for the eventual transfer of all employees to the permanent facility. Utilizing funds made available through the NIH Buildings and Facilities account, construction was begun on the laboratory module in FY 1992 as well as a new chemical waste storage and handling facility. These new additions will provide the Institute with state-of-the-art, safe laboratories.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Detail of Permanent Positions

	1991 Actual	1992 Appropriation	1993 Estimate
ES-5	1	1	1
ES-4	9	9	9
ES-3	1	1	1
Subtotal	11	11	11
GS/GM-15	35	35	35
GS/GM-14	54	55	55
GS/GM-13	48	51	51
GS-12	40	43	43
GS-11	58	61	61
GS-10	2	2	2
GS-9	82	84	84
GS-8	10	10	10
GS-7	58	59	59
GS-6	42	42	42
GS-5	26	26	26
GS-4	16	16	16
Subtotal	471	484	484
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Director Grade	7	7	7
Senior Grade	5	5	5
Full Grade	4	4	4
Subtotal	16	16	16
Ungraded	35	35	35
Total permanent positions	533	546	546

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Advisory and Assistance Services

For FY 1993, the Advisory and Assistance Services budget request will be $255,000, an increase of $10,000 over FY 1992. The emergence of newly recognized environmental issues such as global warming, stratospheric ozone depletion, and hazards from emerging technologies has forced the National Institute of Environmental Health Sciences (NIEHS) to expand the kinds of research it conducts and supports. NIEHS is being asked to embark on such efforts as toxicological studies of compounds used to replace CFCs and to re-examine the relationship between non-ionizing radiation and soft-tissue cancers. This new research can be accomplished more quickly, more precisely, and more cost-effectively if the plans are subjected to careful outside evaluation and pilot tests.

The NIEHS conducts a broad range of basic and applied biomedical research into the potential effects of exposures to environmental hazards on human health. It is critical that design and conduct of these studies and their findings be subjected to rigorous scientific peer review. These peer reviews must be conducted by individuals who possess extensive scientific knowledge and experience in fields as diverse as toxicology, clinical and gross pathology, epidemiology, biostatistics and biomathematics, and all of the sub-specialties of medicine. These individuals must be scientifically expert in their fields, yet at the same time they must be "entirely disinterested." That means that they cannot have or be perceived to have a financial or professional benefit which might accrue to them from the NIEHS study. For this reason, NIEHS staff scientists and scientist-managers, no matter how talented and accomplished they may be, must routinely rely on individual expert consultants to monitor their work and subject it to critical, public review.

At NIEHS the requirement for Advisory and Assistance Services arises almost entirely from the need for scientific peer review. The results of NIEHS studies are used by scientists, engineers, and program managers in regulatory agencies at the State, federal, and international levels. These officials often use data from NIEHS studies in preparing assessments of the risks to human health and ecologic systems posed by man-made or naturally-occurring hazardous substances. These "risk assessments" are used by economists, lawyers, policy makers and elected officials in regulatory and other actions to manage risk and to protect human health and environmental systems.

To ensure appropriate use of consulting services, the NIEHS has established a review procedure involving all appropriate administrative and management personnel. Proposals are reviewed by the pertinent Administrative Officers, the Committee Management Officer, the Budget Officer, the Executive Officer, appropriate program managers, and the Director as necessary. All NIEHS consultants are required to comply with applicable rules regarding conflict of interest. These rules are applied when a consultant is initially hired and re-emphasized at the time the consultant actually performs a specific service to the Institute.

Wednesday, March 1, 1992.

NATIONAL EYE INSTITUTE

WITNESSES

DR. CARL KUPFER, DIRECTOR, NEI
DR. BERNADINE P. HEALY, DIRECTOR, NIH
EDWARD McMANUS, DEPUTY DIRECTOR, NEI
DR. JACK A. McLAUGHLIN, ASSOCIATE DIRECTOR FOR EXTRAMURAL AND COLLABORATIVE PROGRAM, NEI
KENNETH O. COOKE, EXECUTIVE OFFICER, NEI
FREDETTE WEST, BUDGET OFFICER, NEI
DENNIS P. WILLIAMS, DEPUTY ASSISTANT SECRETARY, BUDGET, DHHS

INTRODUCTION OF WITNESSES

Mr. Natcher. At this time, we take up the budget request for fiscal year 1993 for the National Eye Institute. We have before the Committee Dr. Carl Kupfer, the Director.

Dr. Kupfer, it is a pleasure to have you before our Committee. You have been the only director, as I recall, that we have had at the Eye Institute since its creation 22 years ago.

Doctor, you have a good story to tell. You have had a good story to tell all down through the years. As I pointed out the other day when you were sitting in the audience, you are the senior director at the NIH. You may not be the senior as far as service; maybe Dr. Kirchstein has you by a year or two. But you have the longest tenure as a Director, correct?

Dr. Kupfer. Yes, sir.

Mr. Natcher. Tell us who you have at the table.

Dr. Kupfer. To my far left is Mr. Kenneth Cooke, our Executive Officer; next to him is Ms. Fredette West, our Budget Officer; Mr. Edward McManus, the Deputy Director of the Institute; Dr. Jack McLaughlin, our Associate Director for Extramural and Collaborative Program; and, of course, Dr. Healy and Dennis Williams.

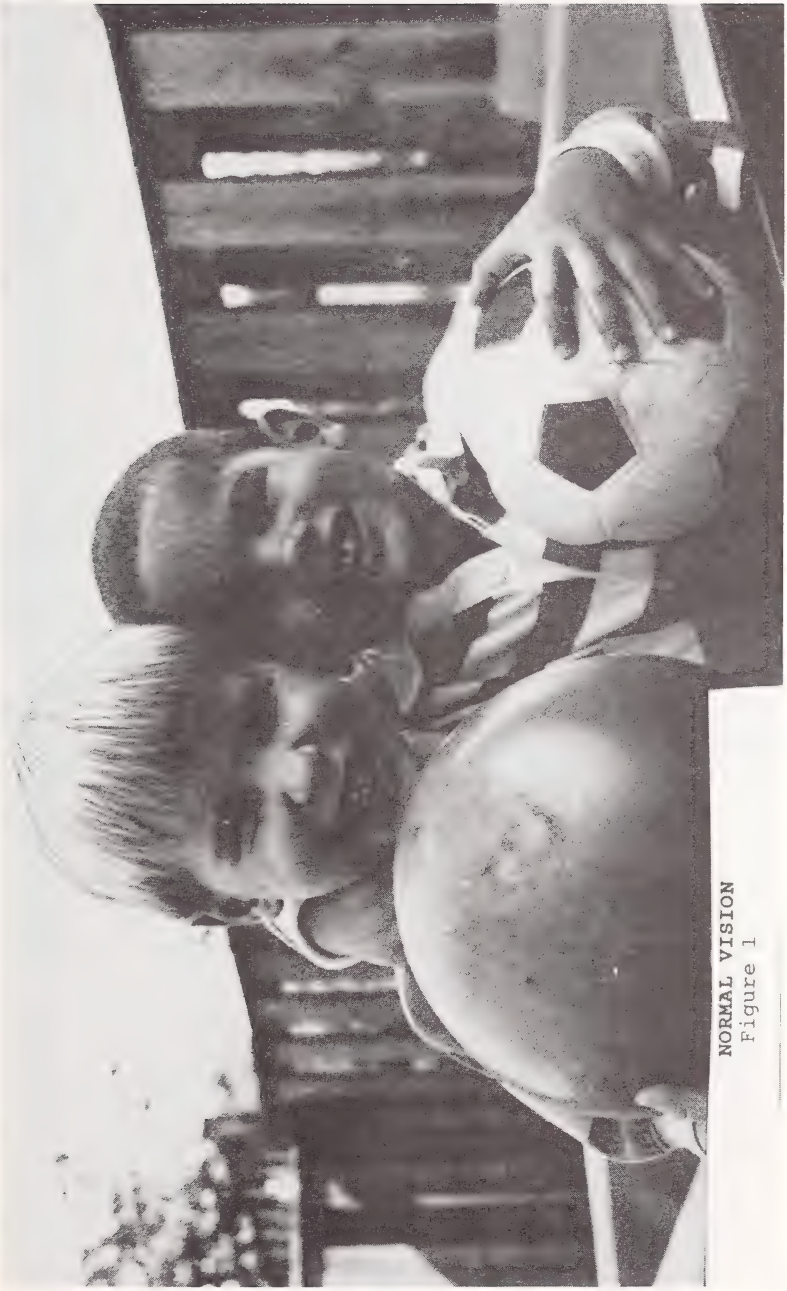
Mr. Natcher. Thank you. We will be pleased to hear from you.

Opening Statement

Dr. Kupfer. Thank you, Mr. Chairman. I would like to call to your attention the increasing age of our American population. What you might not be aware of is that we are perhaps on the verge of an epidemic of visual disability and blindness. There are four major causes; I would like to briefly highlight them.

First, the photograph on the left, in Figure 1, is a very clear photograph of two children. This is what a person with normal vision would be able to see.

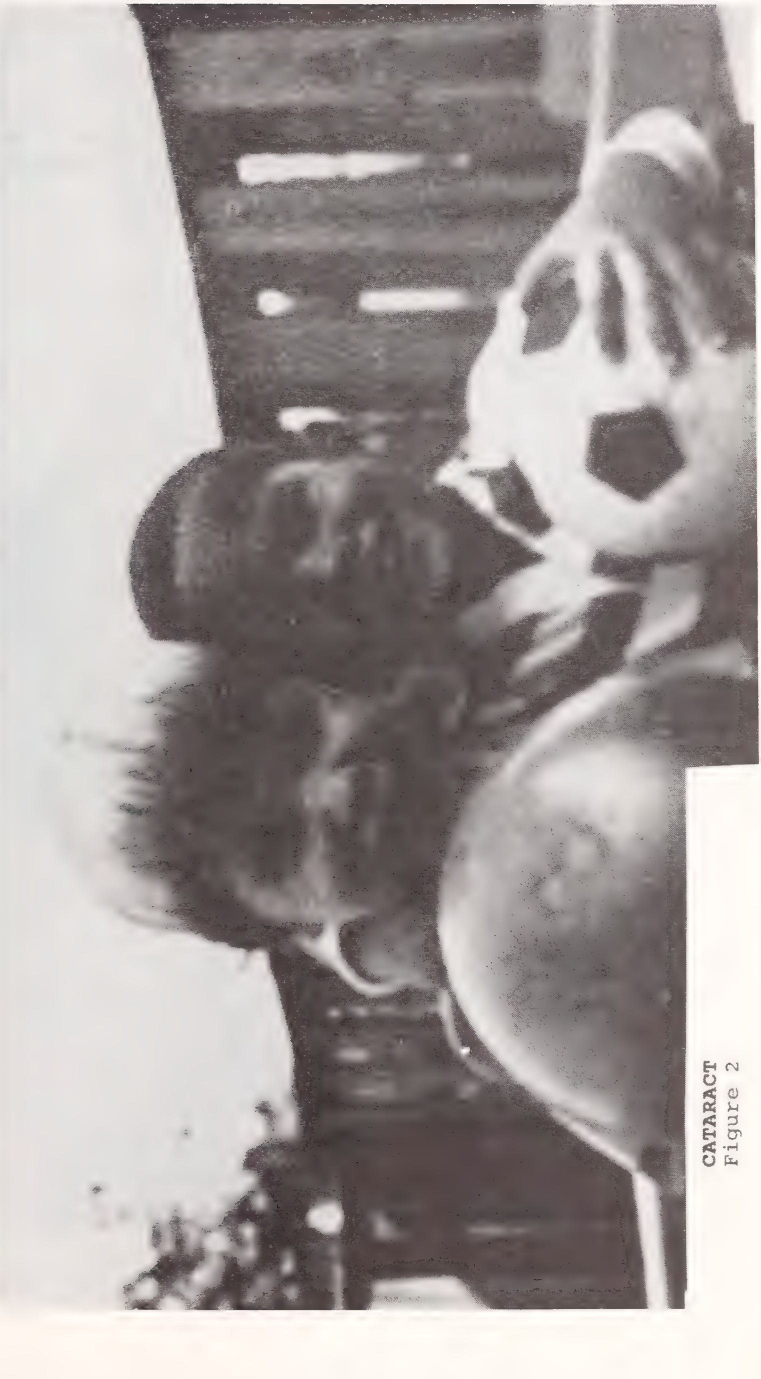
[The information follows:]



NORMAL VISION
Figure 1

At the very earliest stages of cataract, this image becomes very blurred. You will notice in the normal vision photograph, one can see clearly the details of the eyes in the young man on the right, but here, on this photograph, Figure 2, it is quite blurred.

[The information follows:]



CATARACT
Figure 2

This is the earliest sign of cataract, it may be not even noticed by the person undergoing it. But you can imagine how it would interfere with driving or maybe reading the newspapers. That is one of the major problems.

DIABETIC RETINOPATHY

The second is diabetic retinopathy, which the diabetic develops because of bleeding behind the eye. It can eventually lead to blindness. You see its effects on vision in Figure 3.

[The information follows:]

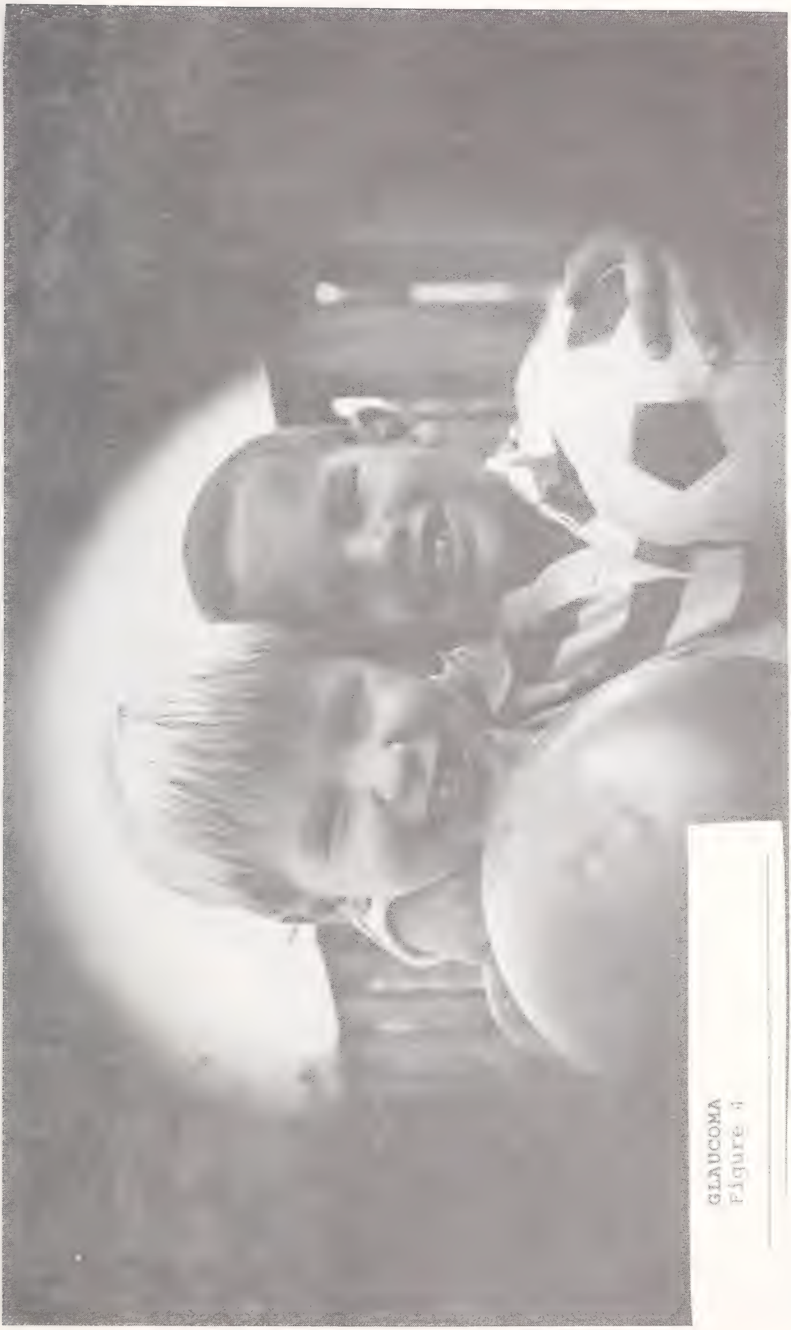
DIABETIC RETINOPATHY
(figure 1

We have made many strides in diabetic retinopathy, but there are many things we have yet to do.

GLAUCOMA

Next is glaucoma. We see the insidious nature of this disease where the central vision is normal, but there is a slow loss of peripheral vision. As this closes in and one develops gun-barrel vision, eventually the center vision is snuffed out. This is shown in Figure 4.

[The information follows:]



GLAUCOMA
Figure 1

In macular degeneration, the initial loss of vision is central vision, so the individual cannot see clearly everything in front of him or her, as shown in Figure 5.

[The information follows:]

MACULAR DEGENERATION
Figure [illegible]

He can see peripherally, but has lost ability to read, watch TV, drive a car, and enjoy the quality of life that the older American should.

We are on the verge of an emerging epidemic in eye disease. We are taking steps to avert this epidemic and to control the loss of vision, and the visual disability that would result from the increased incidence of the four major causes of blindness related to the advancing age of our population.

The request for budget is $285,133,000. I will be happy to respond to questions.

[The statement of Dr. Kupfer follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement of the Director
National Eye Institute

Mr. Chairman, it is a pleasure to testify before this Committee and share with the Members some of the recent accomplishments and ongoing research that are helping us better understand the remarkable complexity of the visual system. This year, I would like to begin my remarks by discussing one of the most formidable challenges to vision research: meeting the current and future eye care needs of our aging society.

Today, there are over 32 million Americans age 65 and older. By the year 2030, this figure will more than double to nearly 66 million Americans. To put this number in perspective, it is greater than the current combined populations of metropolitan New York City, Los Angeles, Chicago, Detroit, Houston, Boston, Washington, D.C., and Philadelphia. With more older people in our society, more Americans than ever will enter our nation's health care system with age-related eye diseases such as cataract, glaucoma, diabetic retinopathy, and macular degeneration. For example, according to our best estimates, about 6.3 million older Americans will develop macular degeneration in the year 2030, compared to an estimated 1.7 million in 1995.

To prevent such increases, the National Eye Institute (NEI) is intensifying its research efforts to determine the fundamental causes of age-related eye disease. We have begun the Age-Related Eye Diseases Study (AREDS), a multicenter clinical research project in which researchers will document in detail the aging process in the eyes of thousands of older Americans. Our hope is that as this study progresses, it will provide us with the scientific basis for the future prevention and treatment of cataract and age-related macular degeneration.

NEI also recognizes that as more older Americans take personal responsibility for helping maintain their eyesight, fewer will suffer the tragedy of losing their vision to a treatable eye disease. To address this issue, NEI recently launched the National Eye Health Education Program (NEHEP), the first Federally sponsored nationwide eye health education program, to promote blindness prevention in Americans at risk for glaucoma and diabetic eye disease, two leading causes of preventable adult blindness. Working in close partnership with 37 private and public organizations, NEI has developed educational materials, including mass media messages, that will encourage millions of Americans at risk for these diseases to protect their vision by having their eyes examined regularly.

As part of this effort, NEI recently issued the first Federal eye care recommendations for people at risk for glaucoma and diabetic eye disease. These guidelines state: People with diabetes should undergo an eye examination through dilated pupils at least once a year; and people at high risk for glaucoma, especially Blacks over age 40 and all people over age 60, should receive an eye examination through dilated pupils every two years.

As evidenced by these guidelines, this education program represents a concerted effort to help protect the sight of older and middle-aged Blacks. This direction was precipitated, in part, by new NEI-supported findings on glaucoma, the leading cause of blindness in Blacks. For example, the Baltimore Eye Survey--the first study to measure glaucoma prevalence in a large racially mixed population--reported last year that Blacks are four to five times more likely than Whites to develop glaucoma. In fact, it found that Blacks tended to get glaucoma earlier than Whites, around age 40, and the disease appeared to progress more rapidly in Blacks.

But, a recent national eye health awareness survey, supported jointly by the NEI and the Lions Clubs International, found that only 20 percent of the Black respondents at high risk for glaucoma said they had seen or heard anything about eye health or eye disease in the past year, excluding advertisements for glasses and contact lenses. Given the high prevalence of glaucoma in Blacks, this finding further highlights the importance of increased eye health education in this group.

A recent study has estimated some of the potential cost-savings that may accrue to the Federal government from the National Eye Health Education Program by increasing awareness of the importance of regular eye examinations for people with diabetes. According to this study, the Federal government is already saving approximately $101 million annually in blindness benefits as a result of the timely examination and treatment of individuals with diabetic retinopathy. As impressive as this may be, however, only an estimated 60 percent of high-risk patients are receiving such sight-saving eye care. It is estimated that if all eligible diabetic patients received appropriate eye care, over $167 million could be saved each year.

The importance of early detection of diabetic eye disease cannot be over-stated since about half of all people with diabetes have at least early signs of diabetic retinopathy. In fact, the NEI-supported Beaver Dam (Wisconsin) Eye Study reported recently that 10 percent of all people newly diagnosed with non-insulin-dependent diabetes already have vision-threatening retinal abnormalities.

By emphasizing the potential savings afforded by eye health education, I do not want to leave the impression that basic laboratory and applied clinical vision research have reached the point of diminishing return--far from it. NEI announced several exciting clinical findings last year that will help raise our nation's standard of eye care. Two of these involve the treatment of cytomegalovirus (CMV) retinitis, a blinding retinal disease that eventually affects about 20 percent of people with AIDS. In the first study, NEI intramural scientists working with other NIH investigators determined that the antiviral drug, foscarnet, is safe and effective in treating CMV retinitis in people with AIDS. This was the first clinical trial to reach such a finding.

The second finding comes from the Foscarnet-Ganciclovir CMV Retinitis Trial, a large, randomized controlled clinical trial conducted at 12 clinical centers nationwide. This study, supported by the NEI with cooperation from the National Institute of Allergy and Infectious Diseases and its AIDS Clinical Trials Group, compared the safety and efficacy of foscarnet and ganciclovir. Ganciclovir was the only FDA-approved treatment for CMV retinitis in patients with AIDS and CMV retinitis when the study began.

Although both drugs appeared to be equally effective in halting the progression of CMV retinitis, trial data indicated that patients treated with foscarnet lived an average of four months longer than those given ganciclovir. The only patients who lived longer on ganciclovir than on foscarnet were those who entered the study with decreased kidney function. This, however, was expected since renal toxicity is a known side effect of foscarnet.

When we ruled out all possibility of statistical or analytical error for the difference in survival, the trial's treatment protocol was suspended and all study investigators and patients across the country were notified of the findings within a week. Because of the important therapeutic implications of these results, the NEI and study investigators simultaneously issued a clinical alert to about 40,000 physicians and others nationwide who work with patients with AIDS. These vital dissemination efforts were completed more than three months prior to publication of a detailed scientific report. A national news conference was also held one week after issuing the clinical alert to inform the public of the finding. I believe this demonstrates that important clinical information can be disseminated in a timely and responsible manner to satisfy the best interests of both doctor and patient alike.

The NEI-supported Optic Neuritis Treatment Trial (ONTT) also reported some highly significant clinical findings. Optic neuritis is an inflammation of the optic nerve that causes temporary vision loss and ocular pain in about 25,000 Americans annually, primarily young and middle-aged women. Without treatment, most people regain near normal vision in a few months but face the possibility of recurrence. But, based on reports that oral corticosteroids improved recovery in patients with optic neuritis, most physicians have treated the disease with these anti-inflammatory agents. The ONTT, a randomized trial conducted at 15 clinical centers nationwide, was the first placebo-controlled study to evaluate whether corticosteroids are in fact safe and effective for this indication.

Trial investigators found that oral corticosteroids alone are ineffective in treating optic neuritis and may actually increase a person's risk for future attacks. Because it would seem logical that a proven class of anti-inflammatory drugs would be an effective treatment for an inflammatory disease of the optic nerve, a possible explanation may be that orally administered corticosteroids do not reach adequate therapeutic levels at the site of the optic nerve inflammation. Indeed, the trial investigators reported that patients who were treated initially with a high dose of intravenous corticosteroids recovered about two weeks sooner than patients given a placebo. Intravenous treatment, however, proved only marginally effective in restoring vision, and patients faced the inconvenience of hospitalization and increased medical costs.

Because of the important therapeutic implications of this finding, the NEI and trial investigators issued a clinical alert more than one month prior to publication of the trial results to ensure that practitioners would have the most current information when treating patients with optic neuritis. The clinical alert was sent to 16,000 ophthalmologists and 11,000 neurologists nationwide.

The past year has also been an extremely productive period in basic vision research. I would like to share briefly with you one particularly exciting finding before concluding my testimony. An NEI grantee recently identified three new gene mutations in patients with autosomal dominant retinitis pigmentosa (RP), one of the most devastating forms of this group of blinding retinal diseases that affects nearly 100,000 Americans. All of the mutations were found in a single gene that had not been previously implicated in RP. Efforts are now underway to determine exactly how these gene defects lead to retinal degeneration, and how to prevent this from happening.

I mention this finding because it is elegant basic research that has a direct bearing on human disease. The human gene defects were identified because of progress that had been made in previous work with a mouse mutant which exhibits similarities to some forms of human RP. In these seminal studies, an NEI-grantee identified and cloned the gene responsible for the retinal defect in the mouse. This then led another NEI-supported scientist in related experiments to identify the human gene, which is very similar to the defective mouse gene. In recent years, some people have questioned the applicability of animal research to the betterment of human health, but as these and numerous other studies document, animal research is invaluable and essential to the advancement of science.

Mr. Chairman, the FY 1993 budget request for the National Eye Institute is $285,133,000. I will be glad to answer any questions that the Committee might have.

KUPFER, DR. CARL
Director, National Eye Institute
February 9, 1928. New York, New York.

Education: A.B., Yale Univ., 1945-48. M.D., The Johns Hopkins Medical School, 1952 Certified. American Board of Ophthalmology, 1958.

Professional History: Internship and Assistant Residency, Wilmer Eye Inst., Johns Hopkins Hospital, 1952-54. Lab. Assistant, Biostatistics, Johns Hopkins School of Medicine, 1953-58. Research Fellow in Ophthalmology, Harvard Medical School, 1958-60. Instructor in Ophthalmology, Harvard Medical School, 1960-62. Assistant Professor of Ophthalmology, Harvard Medical School, 1962-66. Professor and Chairman in Ophthalmology, Univ. of Washington School of Medicine; Research Affiliate, Univ. of Washington Primate Ctr., 1966-70. Director, National Eye Institute, 1970-present. Acting Deputy Director for Intramural Research, NIH, 1991-present.

Professional Organizations: American Physiological Society; Assoc. for Research in Vision and Ophthalmology; American Academy of Ophthalmology; American Ophthalmological Society; Pan American Ophthalmological Society; Johns Hopkins Univ. Soc. of Scholars; Member, Inst. of Medicine, National Academy of Sciences.

Honors and Awards: The Secretary's Special Citation, Dept. of Health, Education and Welfare, 1972; The Superior Service Award, Dept. of Health, Education and Welfare, 1974; Presidential Rank Award of Meritorious Executives, 1983; Migel Medal, Amer. Foundation for the Blind, 1976; Public Service Award in Ophthalmology, Amer. Academy of Ophthalmology and Otolaryngology, 1977; Special Award of Honor, The Assoc. for Research in Vision and Ophthalmology, 1983; David Rumbough Memorial Scientific Award, The Juvenile Diabetes Foundation, 1983; The Lighthouse Pisart Vision Award, 1984; Cavera Medal of Univ. of Rome, 1985; The Mildred Weisenfeld Award for Excellance in Ophthalmology, 1987; Presidential Distinguised Rank Award, 1991.

Other Scientific Activities: Editorial Board, Investigative Ophthalmology, 1969-1977; Editorial Board, American Journal of Ophthalmology, 1971-1983; Member, Scientific Advisory Committee, Fight for Sight, 1971-present; Member, National Diabetes Advisory Board, 1976-present.

International Appointments: Member, Board of Trustees, Helen Keller International Inc., 1975-present; Coordinator for U.S.-Japan Collaborative Agreement in Vision Research, 1976-present; Member, Intl. Vitamin A Consultative Group, WHO, 1973-present; Member of U.S. Delegation to World Health Assembly, 1978; Member, WHO Advisory Group for Prevention of Blindness Prog., 1978-1984; Consultant, Pan American Health Organization, 1978-present; Coordinator for USA, Priority Area "Eye Diseases," U.S.-U.S.S.R. Prog. for Health Cooperation, 1978-present; Member, WHO Expert Advisory Panel on Trachoma and Prevention of Blindness, 1979-present; Dir., WHO Collaborating Ctr. for the Prevention of Blindness, National Eye Inst., Bethesda, MD, 1979-present; Pres., Intl. Agency for the Prevention of Blindness, October 1982-1990.

ACCOMPLISHMENTS

Mr. NATCHER. Thank you.

The Eye Institute will be 25 years old, as you know, in 1993. What would you cite, Doctor, as the two or three most important accomplishments of the Institute since it was created?

Dr. KUPFER. I would have to say that the greatest impact that the National Eye Institute has had is the development of clinical trials to control the blinding diseases associated with diabetes.

We now know that if laser treatment, that we have proven to be effective, is delivered in time, we can reduce by almost 98 percent the number of diabetics who will lose vision. That is a very, very impressive figure. Not only can we reduce blindness, but the dollars that have been saved by having this intervention available from the time the results of the study were published in 1976 to the present amount to as much as $1,200,000,000. I would say this has been a major step forward.

The other accomplishments have been in the establishment of a research base in diseases of the retina, lens, and fluids of the eye which has yielded results that we have transferred to clinical trials, for treatments for other eye diseases like glaucoma and eye diseases of newborns, such as retinopathy of prematurity. I could go on with other advances in clinical research. I think that has been the major impact that the establishment of the National Eye Institute has had on the health of the American people.

INCIDENCE OF EYE DISEASES

Mr. NATCHER. What can you tell us about changes in disease rates for various eye diseases during the period since you have been director?

Dr. KUPFER. I would say the most impressive has been in the area of diabetic retinopathy where we can now detect and treat the early stages of diabetic retinopathy. We can reduce to 1 or 2 percent the diabetics who go blind.

The second is one form of age-related macular degeneration. With laser treatment, we can reduce by about 50 percent those who would go blind from that condition.

I think those two would represent the major impact.

We have advances in corneal transplantation. This is one of the most successful tissue transplant operations. By learning more about the immunology of transplants and the use of new drugs, we can now achieve at least a 95 percent success rate in the vast majority of cases.

Finally, we have made strides in the diagnosis and treatment of inflammation of the eye, uveitis. With new drugs, we can suppress the immune reaction so the body mobilizes its own defenses to overcome the inflammatory condition.

NATIONAL EYE HEALTH EDUCATION PROGRAM

Mr. NATCHER. Last year the Eye Health Program was officially launched. What can you tell us about the current focus of this effort and your plans as far as the future are concerned?

Dr. KUPFER. We have been very happy about this program, which has moved into the community outreach. We now have 40 organizations that have signed on as partners in this program, and more will join soon.

We have held focus groups to find out what are the current knowledge and information needs of small groups of people with diabetic eye disease and glaucoma. We mounted a national survey of Americans' knowledge, attitudes, and practices with respect to eye diseases and eye health. It was partially funded by the International Lions Clubs. We have really begun to launch programs where materials we developed are going out into the community. We have initially targeted high-risk groups for glaucoma and for diabetic eye diseases. Material has been produced and disseminated, and we have in place a truly national program.

I have great hopes this will have a major impact. What lies ahead, of course, is to evaluate the impact of these public health education activities to be sure that they have a major impact, especially on the population groups that are at highest risk.

Mr. NATCHER. How much money is budgeted for this education effort in 1992 and 1993?

Dr. KUPFER. In 1992, it is approximately $2,900,000; and in 1993, it is a shade more than that.

SUCCESS RATE

Mr. NATCHER. Dr. Kupfer, your Institute has always had a reputation as one of the best-managed at NIH. As we review your budget request for 1993, there appears to be a pretty stable situation in terms of numbers and cost of grants.

Despite this stability, there appears to be a significant decline in the success rate for applications at the Eye Institute. This rate was nearly 50 percent in 1987. This declined to 27 percent in 1993. What about this problem?

Dr. KUPFER. Well, sir, I think much has to do with the fact that we are seeing an increasing number of research grant applications come into the National Eye Institute. As more and more grants are submitted, obviously the success rate, which is the number of applications funded divided by the number reviewed, will tend to fall unless we could fund more than were actually going to be funded.

I think part of the problem is that we have been very successful in attracting researchers into the vision field. They see the opportunities. They see the advantages that working on the visual system yield, and they see that the approach to certain problems of even broader health significance can be best accomplished in this organization and system.

RESEARCH CENTERS

Mr. NATCHER. The Eye Institute has always had the majority of its budget within the research project grants mechanism. Why do you view research centers as a less important mechanism?

Dr. KUPFER. In a sense, we have centers, but they are of a different nature. If one goes to a university—to the departments of ophthalmology, physiology, pharmacology, biochemistry—one might find that the National Eye Institute would be supporting 40 or 50 research grants. We could say that university represents a center. However, each individual investigator has his or her own research grant. We say, because there is such a large number of individual researchers doing work on the visual system, we will provide a center core grant to give each of the individuals the opportunity to access a central machine shop, tissue culture facility, or whatever would enhance their own research activity.

We have always felt that the best way to support the best researchers is through the individual investigator-initiated research grant. But there are many, many institutions that have 10, 20, 30, research grants, and one could easily say that they, in a sense, represent our "centers." It is just that we have approached it in a different manner.

CLINICAL TRIALS

Mr. NATCHER. The budget mechanism tables show a large increase in 1992 for clinical trials, which increase about $5,700,000 this year. Last year, you expected this increase to take place in 1991. Why have these trials been delayed, Doctor?

Dr. KUPFER. The glaucoma trial which we were planning to fund had to be delayed temporarily.

Mr. NATCHER. Are you, in general, satisfied with the proportion of your budget in clinical trials?

Dr. KUPFER. Yes, sir. I think the amount is really determined by the opportunities. We have a very large research base that represents laboratory research. From this research base, opportunities come up for us to transfer what is learned in the laboratory to the bedside.

Now, as you can see, funding from 1992 to 1993 will be level in the clinical trial line. So we will be keeping the support of clinical trials at the same level.

GLAUCOMA

Mr. NATCHER. Mr. Stokes, I yield.

Mr. STOKES. Thank you, Mr. Chairman.

Dr. Kupfer, in your Institute's justifications on Page 85, you made this statement: "Glaucoma in blacks: Recently published results from the NEI-supported Baltimore Eye Study revealed that the prevalence of glaucoma among black Americans is four to five times that of whites. Glaucoma has progressed more rapidly in blacks."

Then, I find this interesting, "These differences were not related to socioeconomic status or to access to or use of eye care services."

Can you explain that for us?

Dr. KUPFER. Yes, sir, the study was conducted in an area of the eastern health district which is within 10 or 15 miles of John Hopkins Hospital, good facilities were available.

There were no differences between whites and blacks as far as the socioeconomic circumstances were concerned. Therefore, it was appropriate to compare glaucoma rates in these two groups, and the investigators found that there was a very much higher prevalence of glaucoma in blacks.

If one looks at this situation worldwide, there is no doubt now—and this was the first study to document this—there is no doubt that open-angle glaucoma is more prevalent in blacks than whites, here, in the Caribbean, or elsewhere. We are either dealing with a more virulent form of the disease in blacks or a different disease that occurs at an earlier age.

We are studying these differences further to determine what is the situation. Because of this, through the National Eye Health Education Program we have identified glaucoma as a very high priority, and we have appealed directly to the black communities, to all blacks over the age of 40, to have yearly eye examinations with a dilated eye to pick up early signs of glaucoma.

GLAUCOMA TREATMENTS

Mr. STOKES. Where it is diagnosed early, what can be done?

Dr. KUPFER. There are three approaches. The most conservative is the use of eye drops. A recently completed clinical trial showed that if one compares the use of laser treatment with the use of eye drops as the initial treatment of glaucoma, that the laser treatment compares favorably and does initially eliminate the need to put in drops two or three times a day.

The third intervention, which we are very much interested in, is surgical treatment. The reason for that is that once surgery is done by a well trained surgeon at an early stage, the patient may go for five to ten years without any medication and without loss of function.

We must determine what is in the best interest of the patient; should we begin with medicine, drops, immediately go to the laser, or start with a surgical procedure?

Mr. STOKES. In terms of your budget and this particular problem, how is it reflected in terms of the funding you are devoting to the research in this area?

Dr. KUPFER. This is a very high priority and has been for the past ten years. We are spending about $24,000,000 in this area and we are taking advantage of the research opportunities, including the question of glaucoma and blacks.

AGE-RELATED MACULAR DEGENERATION

Mr. STOKES. You talked earlier when you had your graphs up there about AMD and the onset of it. Do we know now what the factors are that contribute to the onset of AMD, other than age?

Dr. KUPFER. Certainly age is the greatest risk factor, but in terms of the specific mechanism, there are two forms. The wet form occurs when abnormal blood vessels grow under the retina, hemorrhage, and destroy it. The other form is the dry form, in which a single layer of cells that ordinarily nourish the retina die for reasons that are unclear, and then the retina dies.

We think the basis for the second form may be what is referred to as oxidative stress. That is the sort of stress that a number of environmental factors or nutritional factors may place as an individual ages.

The first form, where there are new vessels, probably is related to some stimulus that causes the vessels to grow, and that is being studied aggressively. Even so, we are not sure of the mechanism.

Mr. Stokes, we have initiated a clinical trial to examine nutritional factors, vitamins and minerals, as to whether they may slow the development of age-related macular degeneration. Sometimes when knowing the mechanism, one can begin to look for a treatment.

We did not know the mechanism of diabetic retinopathy, but we now know how to treat it.

DIABETES STUDY

Mr. STOKES. We talk about diabetes related to the cause of blindness. A study was done in Wisconsin. What were some of the findings of that study?

Dr. KUPFER. It was done to document the diabetic eye disease of a population with diabetes. We now have a guide to finding what happens to the eye of an individual when he or she has diabetes.

What happened in that study and what galvanized us into getting into the education program was the finding that 50 percent of the diabetics in the Wisconsin study had not had an eye examination in the past two years. We have a treatment we know is almost 95 percent effective, and yet 50 percent of the diabetics had not received an eye examination.

This has focused our attention on having the people in the study continued to be followed by the program and told to get an examination every year after their diagnosis of diabetes. I think we can significantly reduce the number of people losing sight because of diabetes.

Mr. STOKES. How about increased high blood pressure?

Dr. KUPFER. Yes, sir. One of the causes diabetic eye diseage is elevated blood pressure. Therefore, the individuals in the study are being told by the doctors to reduce blood pressure and are on medication for this.

LOW BIRTH-WEIGHT INFANTS

Mr. STOKES. Dr. Kupfer, with improvements in neonatal care over the past two decades, more premature infants, including an increasing number of high-risk, very low-birth weight babies, are surviving. The incidence of retinopathy of prematurity has increased and this is now the leading cause of blindness for premature babies.

To what extent are we seeing an increase in this type of blindness?

Dr. KUPFER. Yes, sir. One of the causes of diabetic eye disease is have become more skilled in keeping these small young babies alive, the possibility of their becoming blind increases. We have made some major strides with a clinical trial that showed that if we freeze the peripheral part of the retina early on, as soon as there is evidence of a retinopathy of prematurity, we can reduce by 50 percent the number of infants that will go blind.

As to the other 50 percent, we are contemplating a new clinical trial to see whether doing further surgery can cure the retinal detachment that occurs in these very premature infants.

Trying to keep up with the increasing number of babies that are born with very, very low birth weights—and I am talking about a thousand grams or less—we are very actively becoming involved in other ways to slow the development of retinopathy.

There are two clinical trials in the development stage: one, to look at the question of whether excessive exposure to light early on is a risk factor. If you go into a premature nursery, the lights are very, very bright because the nurses have to give intense care to these tiny infants in incubators and they need a high level of light.

We know prolonged exposure to high levels of oxygen will cause retinopathy of prematurity, but oxygen also keeps these infants alive. Can we find a level of oxygen that will keep the infants alive, but not cause retinopathy of prematurity?

From the recent clinical trial that we have done in which we saved 50 percent of infants from going blind, we have calculated that we are saving $40,000,000 to $60,000,000 a year over the life of that infant in not having to provide special care, education vocational rehabilitation and other benefits. The findings from the trial are important from a public health point of view and also from an economic impact point of view.

Mr. STOKES. To what extent is research in this area reflected in your budget?

Dr. KUPFER. The major thrust that we would like to pursue would be expanding our clinical trials. We have the questions that need to be asked. At the moment, our clinical trial budget is level and I think we will have to look at our internal management to see whether we can free up funds to pursue these opportunities.

Mr. STOKES. Thank you, Dr. Kupfer.

CATARACT

Mr. NATCHER. Now, Dr. Kupfer, according to your statement, this country spends about $5,000,000,000 per year on cataract surgery. Has there been any progress in developing alternative treatments or prevention methods for this problem?

Dr. KUPFER. This is a very high priority area, not only for the National Eye Institute, but I think in the pharmaceutical sector, to try to develop drugs that will slow down the development of cataracts.

We now must test a hypothesis to see if it stands up to experimental design. If it does, we will then know what mechanisms are operative and be able to design drugs that will interfere with development of cataracts.

The lens of the eye is perhaps one of the best indicators of biological aging, and when the clear lens becomes opaque, this may represent a change that occurs when a normal aging process suddenly becomes abnormal.

I think through cataract research we are not only going to have an impact on the development of cataract and slowing its progression, but will address the question of the aging process in general.

ALLOCATION OF FUNDING

Mr. NATCHER. When the Institute allocates funding, how do you factor economic considerations into these decisions, Doctor?

Dr. KUPFER. First of all, we are always interested in maintaining a strong research base from which our clinical applications come. Secondly, the applications must be of public health importance.

If you look at our clinical trial portfolio, we are working in areas that are affecting large numbers of people or are affecting a small group of individuals, but have a major impact on quality of life, such as the blindness that occurs in infants. They are going to be blind for the rest of their lives.

So, we do look at the impact of the public health problem and that is our major criterion.

However, we are also aware of the need to assess the economic impact of the clinical research we do. We think we are able to do that very well.

There is another aspect I think I should bring to your attention. We have established relationships with industry in which private firms invest in our clinical trials. I mentioned the study of age-related macular degeneration and cataract.

We have the clinical trial portion of that study fully funded by the private sector, and I think from the American people's point of view, this is a very good investment. The private sector will also profit by being able to show that their new drug or device is solid, and we can do a clinical trial that we would not have had the resources to do.

NEI FIVE-YEAR RESEARCH PLAN

Mr. NATCHER. What is the current status of efforts to update the five-year research plan for the Eye Institute?

Dr. KUPFER. We are in the final stages of putting together the final document. We have been particularly concerned with the fact that the pace of research is so rapid that if it takes a year or two or three to develop a five-year plan, by the time one is about to publish, many of the activities are no longer valid.

So what we have done is continually update as we are preparing the final document by circulating drafts to the leaders in the field, including proposed priorities, and I would say by this late spring, May, we will have the final document in place.

The important thing is that it will be up to date.

TRANSFER OF NCI FUNDS

Mr. NATCHER. Dr. Kupfer, last year Congress permitted the Director to transfer funds from the Cancer Institute to cancer studies conducted by other institutes.

Did the Eye Institute receive any of this money?

Dr. KUPFER. Yes, sir. We received $1,000,000.

Mr. NATCHER. What type of cancer research projects do you expect to support with these funds?

Dr. KUPFER. About five years ago, some of our vision researchers were able to finally show that the cause of a eye cancer called retinoblastoma was due not to a gene that causes cancer, but to the absence of a gene that prevents a cancer from developing.

In other words, the gene had to be absent for the cancer to develop. That gene was characterized and the protein that it produces was identified. It was found to play a role, not only in the cancer of the eye, but in cancer of the prostate, breast cancer, and bone cancer. That completely opened up the field of cancer biology.

This is one of the most exciting discoveries that has been made in the last decade. We support research in retinoblastoma because we are interested in developing ways to prevent this life-threatening tumor from developing in newborns and young children.

FETAL CELL TRANSPLANATION

Mr. NATCHER. As you know, there has been a great deal of interest in fetal cell transplantation research related to blindness.

What is your professional judgment about the value of these studies?

Dr. KUPFER. I think at the present time our major thrust should be to document the effect of such tissue in the experimental animal. I think that has been our major direction of research along these lines. I think the major thing that we are looking at is ways of allowing the central nervous system—in other words the brain and the spinal cord—and the optic nerve, which is part of the brain, to regenerate when it is injured.

If one injures a peripheral nerve in the arm, it will grow back, but if one injures the central nervous system, it will not.

We want to know how to unlock the cause of why central nervous system tissue doesn't regenerate. We think we know that very early on, certainly at birth or very soon after, there is the potential of regeneration, but that is quickly lost, and we would like to bring it back.

There is exciting animal work going on looking at the effects of growth factors and various other factors that are intrinsic to fetal tissue in the development of regeneration, but it is well needed to document this in the experimental mammal.

Mr. NATCHER. Does the Eye Institute support these studies or is it private money?

Dr. KUPFER. We follow the Administration's policy by not funding that area of research. The private sector does support some fetal tissue research in humans.

STAFFING

Mr. NATCHER. How many full-time equivalent positions are currently authorized for the Eye Institute and how do you expect this to change in 1993?

Dr. KUPFER. In 1992, there are 247 full-time equivalents. In 1993, 255 are being requested.

Mr. NATCHER. The history tables show an increase of almost 20 percent in staffing for the Institute in the last five years. Are these people all necessary, Dr. Kupfer?

Dr. KUPFER. Mr. Chairman, I would say that the National Eye Institute is one of the leanest institutes in terms of staffing patterns. I think many of the individuals were recruited to take advantage of certain research opportunities in our intramural program. We are given the mandate to develop a National Eye Health Education program and that required some positions and, of course, the impetus to increase activity in the AIDS area accounts for increasing positions.

ARTIFICIAL VISION TECHNOLOGY

Mr. NATCHER. Last week the Committee heard testimony about the potential to develop artificial vision devices for blind people.

This research was very impressive but seemed primitive, Dr. Kupfer.

What is your own view of the practical potential for this technology?

Dr. KUPFER. It is always easy to underestimate the power of technologic development. There is no doubt if there was a convenient way to translate an image into a stimulus to a blind person that they would be able to walk about and ambulate, this would be a major advance. I think we must leave it to the investigators who have committed themselves to pursue this type of research and the very brave patients who are willing to become involved in this research to answer the question whether it is going to turn out to be feasible.

TRACHOMA

Mr. NATCHER. Mr. Stokes, I yield.

Mr. STOKES. Thank you, Mr. Chairman.

Doctor, looking through your justifications, I see that trachoma, which is an infectious blindness, appears to be one of the most readily preventable causes of blindness, yet it continues to spread, for some reason.

Can you tell us about that?

Dr. KUPFER. Yes, it is caused by an infectious organism, some forms of which are sexually transmitted, and it has become much more prevalent in the United States. Interestingly, from a historical point of view, trachoma was usually associated with the developing world as a major cause of blinding eye disease, and over the last 60 or 70 years, it had not caused any significant number of cases of blinding eye diseases in the United States. But it has reemerged as a major result of sexually transmitted disease.

The major problem is that children born of mothers with the infection often develop severe pulmonary and gastrointestinal symptoms. It can also cause eye infections in newborns of mothers who have this disease.

We have just concluded a study which shows that with good prenatal care, this particular infection could be completely done away with.

I think that is the way to approach it. We hope in the future there could be one or two groups that will be very active in developing a vaccine that would not only have a major impact on the disease in the United States, but worldwide.

HERPES

Mr. STOKES. There is something called ocular herpes that is similar but attacks nerve cells; is that correct?

Dr. KUPFER. Yes, sir. Probably most of us harbor the herpes virus and often its most common manifestation is the cold sore in the mouth.

Unfortunately, some individuals develop herpes infection in the eye and if it takes up residence in the nerves supplying the eye, this can be debilitating in terms of pain and in terms of days lost from work.

We have just completed a clinical trial of medication in the treatment of more superficial cases of herpes and are looking at ways of treating herpes once it has taken up residence in the eye nerve tissue.

This is another clinical trial that I think is addressing a major problem. Herpes is a sexually transmitted disease that manifests itself in organs other than the eye.

Mr. Stokes. Are you trying to develop a vaccine in this area?

Dr. Kupfer. Yes, and there is a drug, acyclovir, which is of some benefit in reducing the severity of the disease.

MINORITY EMPLOYMENT

Mr. Stokes. In light of some of these concerns we have talked about in terms of minorities, and the way they are affected, do you have on your staff a high percentage or a low percentage of minorities employed?

Dr. Kupfer. I would say that we have a good balance between minorities and non-minorities. We are always interested in hiring well-qualified individuals. I personally have had a long-standing relationship with Howard Medical School, with Dr. Claude Cowan, who is there at the present time, and we are very anxious to increase the number of minorities in our intramural program.

I think extramurally we have done moderately well, but we continue to have discussions and try to bring people on who would function in our intramural program as well as in the departments of ophthalmology and basic science departments at universities.

In terms of specific numbers, I can tell you that out of a total of 85 GS/GM 13–15 and staff fellow positions, 18 are minorities. If one looks at senior staff fellows, the percentage of minorities would be about 26 percent; medical officers, 25 percent; GS–14 to GS–15, 17 percent; and staff fellows would be about 40 percent, but I still feel that these figures can be improved.

Mr. Stokes. I would appreciate it if you would give me an accurate accounting in the record with reference to minorities on the staff and positions, grade levels and so forth.

[The information follows:]

Detail of Minority Positions
As of March, 1992

In fiscal year 1992, the Institute expects to support a total of 167 GS (general schedule) and GM (general merit) positions and about 29 staff fellows. It is important to note that NEI does not maintain a record of positions by race or ethnic group. As such, the data provided is only an estimate at best. It is against this backdrop that we provide the following distributions. Currently, there are 48 minorities on staff in NEI: 39 in GS/GM positions and 9 in staff fellow positions. In total, 31 minorities are in research positions: 22 in the GS-5 to -14 position and 9 staff fellows. Minorities represented includes: African Americans, Asians, and American Native Indians. The chart below provides an estimated detail distribution by GS, GM, and staff fellow positions.

Estimate Positions Distribution

Category	Total of Positions	No. of Minority	Percent of Total	No. of Minorities Research	Percent of Total
GS/GM-15	20	1	5.0%		0.0%
GS/GM-14	22	5	22.7	4	18.2
GS/GM-13	19		0.0		0.0
GS-12	18	3	16.7	1	5.6
GS-11	21	5	23.8	5	23.8
GS-10	1		0.0		0.0
GS-9	21	6	28.6	6	28.6
GS-8	7	4	57.1	2	28.6
GS-7	21	6	28.6	1	4.8
GS-6	8	1	12.5		0.0
GS-5	5	5	100.0	3	60.0
GS-4	2	2	100.0		0.0
GS-3	1	1	100.0		0.0
GS-2	1		0.0		0.0
Subtotal	167	39	23.4	22	13.2
Senior Staff Fellows	19	5	26.3	5	26.3
Staff Fellows	10	4	40.0	4	40.0
Subtotal	29	9	31.0	9	31.0
Total	196	48	24.5	31	15.8

OFFICE OF MINORITY HEALTH

Mr. Stokes. To what extent does your Institute work with the Office of Minority Health?

Dr. Kupfer. We certainly work with Dr. John Ruffin and are concerned with central NIH minority programs and participate in them, but I think it is important that we at the NEI take things in our own hands and make a definite effort to identify and try to recruit the very best people from minority groups into vision research.

We have always done that, historically. But we do look to Dr. Ruffin for overall guidance and for the development of innovative programs, and we would certainly want to participate in new initiatives in this area. We would want to work as full partners.

Of course, joint funding with the Office of Minority Health will be a very important factor in being able to accomplish these goals.

Mr. Stokes. I agree that each Institute should have its own specific targeted programs relative to some of these minority problems we have discussed. I guess in that vein, one of my greatest concerns is that we continue to hear of this disparity in these types of diseases as they relate to African Americans. It seems to me that overall there has to be some greater concentration on how to eradicate the disparity that exists between Americans, depending upon their race or color.

So that is why in each Institute I am concerned about, not only the liaison you have with the Office of Minority Health, but how effectively you are developing your own programs to intensify research and clinical trials, et cetera.

Dr. Kupfer. I agree with you completely. Of course, Dr. Ruffin may be able to provide additional funds for each of the Institutes and that would be very valuable. I think we have participated in the different NIH programs that have been ongoing, as well as the ones that he is beginning.

More important, a major thrust of the NEHEP is to the black community, not only in the area of glaucoma, where it is the major target group, but even in terms of diabetes, where blacks are at much greater risk.

I agree and we will continue to work very hard in this direction.

Mr. Stokes. Thank you very much, Dr. Kupfer.

Mr. Natcher. Dr. Kupfer, we want to thank you and your associates for appearing before our Committee at this time on behalf of your budget request for fiscal year 1993.

Dr. Kupfer, this has been a good hearing just like it always is. You are a good director, Dr. Kupfer, and it is a pleasure to have you before the Committee, and this applies to all your associates.

The Committee will now adjourn until ten o'clock in the morning.

[The following questions were submitted to be answered for the record:]

AGE-RELATED MACULAR DEGENERATION

Mr. Roybal: Is age-related macular degeneration a significant problem among older Americans? If so, to what degree?

Dr. Kupfer: Age-related macular degeneration (AMD) is an eye disease that destroys cells in the small specialized area of the central retina which is responsible for sharp, crisp vision. As the disease progresses, the ability to read, drive a car, and to perform other daily activities steadily diminishes. AMD is an important and growing public health problem in older Americans. By 1995, it is estimated that 1.7 million Americans will have decreased vision from AMD, and 100,000 will be blind from the disease. The prevalence of AMD is expected to rise to 6.3 million by the year 2030, when an even greater percentage of our population enters its retirement years.

AGE-RELATED EYE DISEASES

Mr. Roybal: Are there eye diseases other than age-related macular degeneration that are prevalent in the elderly population?

Dr. Kupfer: Yes, aside from age-related macular degeneration included among the diseases of the eye that result in blindness or reduced vision as a result of aging are aging-related cataract and glaucoma. These age-dependent eye disorders are common causes of visual loss in the United States. In addition, the longer one has had diabetes, in general the greater ones chances are of developing diabetic retinopathy. Age-related eye disorders will become even more important in coming decades since the elderly are the fastest growing segment of the population.

Mr. Roybal: What percent of the elderly population suffers from eye disease?

Dr. Kupfer: A great many diseases and disorders of the eye are associated with aging, including age-related macular degeneration, diabetic retinopathy age-related cataract, and glaucoma. Estimates for age-related macular degeneration alone indicate that nearly 1.7 million people--about five percent of those age 65 and older--will have the disease in 1995. Although the percentage of the elderly suffering from all eye diseases is not known, it has been estimated that more than half of all visual impairment in the United States occurs in this age group.

Mr. Roybal: What is the projected number of elderly Americans who will suffer from eye disease given the rapidly growing elderly population?

Dr. Kupfer: It is estimated that the number of Americans age 65 and older will more than double from its current 32 million by the year 2030. A significant increase in all aging-related diseases and disorders of the eye are expected in this group. Age-related macular disease, for example, is expected to be present in 10 percent of those age 65 and older by 2030.

AGE-RELATED MACULAR DEGENERATION

Mr. Roybal: Would you provide the Committee a description and the funding level of the current age-related macular degeneration research being conducted by the National Eye Institute?

Dr. Kupfer: Research initiatives in a variety of age-related macular degeneration projects are underway:

Macular Photocoagulation Study. A series of NEI-supported, randomized, multicenter clinical trials, the Macular Photocoagulation Study (MPS), has demonstrated the effectiveness of laser treatment of leaking blood vessels just outside the center of the macula in reducing the rate of visual loss from the "wet" form of AMD. However, clinicians have been uncertain about whether it would be beneficial and safe to treat blood vessels which grow directly beneath the center of the macula. The MPS group has recently reported that laser photocoagulation of these lesions was effective two years after treatment in delaying or preventing deterioration of visual acuity and other measures of visual function. These new results have extended the treatment eligibility range considerably to include patients who suffer from some of the most severe manifestations of AMD.

Age-Related Eye Diseases Study. An NEI-initiated study to learn more about how AMD and cataract develop and progress, the Age-Related Eye Diseases Study (AREDS) is well underway. AREDS, which will include more than 4,600 volunteers throughout the Nation, will be the first large-scale attempt to follow the clinical course of these two eye diseases. In addition, the possible role of nutritional supplements and minerals in delaying the development and progression of these two eye diseases will be evaluated in a randomized clinical trial.

Molecular Mechanisms of AMD. Although the cause of this disease is unknown, it is thought to be caused in part by abnormal trafficking of metabolites and cell materials through the retina or a disruption of cell-cell communication which is important for cell function in the macula. Laboratory studies show that lipids accumulate with age in Bruch's membrane, which is located between the retinal pigment epithelium (RPE) and the underlying layer of blood vessels called the choroid, disrupting its structure and altering its fluid permeability. Deposits called lipofuscin accumulate with age in the RPE, and it is thought that such accumulation of material may compromise the health of the cell and lead to altered function. It has been shown that under cell culture conditions, the RPE of the macula differs from that of the peripheral retina. The search for RPE-specific proteins using the modern technology of molecular biology is currently an active area of investigation.

Current fiscal year NEI funding level for macular degeneration is an estimated $57.8 million.

AGE-RELATED EYE DISEASE--FUNDING

Mr. Roybal: Are there any age-related research programs authorized in FY 1992 which were not funded?

Dr. Kupfer: Basic and clinical research in age-related eye diseases remain one of the NEI's highest priorities. Since scientific progress, by its very nature, produces new opportunities there are always opportunities ready to be exploited that are going unmet. However, within the funds available, NEI is supporting those projects which it considers to be among the highest priority.

AGE-RELATED EYE DISEASE--OPPORTUNITIES AND FUNDING

Mr. Roybal: Similarly, are there research opportunities which could be expanded in FY 93 and at what funding level?

Dr. Kupfer: Yes, there are new research opportunities ready to be exploited in areas including age-related macular degeneration, cataract, glaucoma, and diabetic eye disease. The professional judgement estimated cost for this expansion is $89.3 million. However, for any further program increases beyond those included in the FY 1993 President's budget, no further offsets have been identified to support them within the agreed-upon levels of funding under the Budget Enforcement Act.

Mr. Roybal: Are there new age-related research programs focusing on the elderly and eye disease which should be initiated in FY 93?

Dr. Kupfer: If additional resources became available to support activities beyond those high priority projects included in the FY 1993 President's budget request then the following initiatives should be considered:

Age-Related Macular Degeneration: expansion of basic research on the retina to identify genetic, nutritional, or other age-related changes in the retina which contribute to the development of AMD; further exploration of transplantation techniques, use of growth factors and other approaches for rescuing degenerating retinal cells; characterization of biological factors and inhibitors to prevent the development of abnormal blood vessels in AMD; and, launching new clinical trials to determine the effectiveness of vitamins, nutritional supplements, and minerals in preventing or treating AMD.

Glaucoma: expanded basic and clinical research on the molecular mechanisms of fluid production and transport in the eye and on the cause of optic nerve damage in glaucoma; research to determine why the rate of glaucoma is higher and the disease possibly more severe in Blacks; the development of better noninvasive methods for evaluating the health of the optic nerve; the development of new drugs and biologics to control intraocular pressure; and additional clinical trials of glaucoma treatments.

Diabetic Retinopathy: accelerated research on the cell biology of the retina, including research on newly discovered growth factors which may play a role in the development of abnormal and destructive retinal blood vessels; development of new drugs and molecular genetic techniques to inhibit aldose reductase, the enzyme involved in the pathogenesis of diabetic retinopathy; studies to understand how blood flow is regulated in the retina; and clinical investigations to assess risk factors for the severity and progression of diabetic retinopathy.

Cataract: intensified and expanded efforts to develop effective strategies to prevent or delay the formation of cataracts; investigations of ways to augment the lens's natural defense mechanisms, which prevent or retard cataract formation; molecular genetic studies to determine how the genetic expression of lens-specific proteins is regulated and biochemical studies to determine the critical changes in lens proteins that occur with age; clinical studies to evaluate the safety and efficacy of anticataract drugs and methods of clinical management.

HIGH PRIORITY AGING RESEARCH INITIATIVE IN VISION

Mr. Roybal: How much money would be necessary to fund these programs?

Dr. Kupfer: In my professional judgement, a total of $89.3 million over the FY 1992 budget would be necessary to fund them. The FY 1993 President's budget includes an increase of $14.8 million, a 5.5% increase over FY 1992.

Mr. Roybal: Considering both expanded existing research projects and the initiation of new programs on age-related research on eye disease among the elderly, in FY 1993, how much would it cost to support both old and new programs?

Dr. Kupfer: The combined cost to maintain existing programs and to implement these new initiatives would total about $359.6 million, a 33% increase over FY 1992.

Mr. Roybal: Is research in the area of age-related eye disease a high priority at NIH which would be expanded if additional funds were provided over the President's request?

Dr. Kupfer: Yes, aging research is included among the high priority initiatives in the NIH strategic plan and as such, is targeted for expansion. There are many outstanding research opportunities in age-related eye diseases to address the sight-robbing eye diseases that continue to undermine the quality of life of millions of older Americans and place an enormous economic burden on families, their communities, and the Nation.

COLLABORATION IN AGING RESEARCH

Mr. Roybal: Is there currently any research collaboration between the other Institutes and NEI which focus on aging?

Dr. Kupfer: Several such collaborations are underway. For example, NEI joined with the National Cancer Institute and the

Cancer Institute of the Chinese Academy of Medical Sciences, to conduct eye examinations in central China at the end of a five-year randomized trial of vitamin/mineral dietary supplements. Almost 6,000 adults were examined to see if that nutritional intervention might reduce the occurrence of age-related cataract and age-related macular degeneration. Data analysis is in progress.

OPPORTUNITIES FOR CLINICAL BREAKTHROUGHS

Mr. Stokes: The budget document indicates that in the area of vision research, opportunities abound for making advances which will improve the prevention, detection, and treatment of visual disorders.

What basic science areas of vision research hold the greatest potential for clinical breakthroughs?

Dr. Kupfer: The conduct of basic research in a broad spectrum of crosscutting areas in vision research holds tremendous potential for clinical breakthroughs. Among these areas are: expanded basic research on the retina to identify genetic, nutritional, or other age-related changes that contribute to the development of macular degeneration; further exploration of transplantation techniques, use of growth factors, and other approaches for rescuing degenerating retinal cells; and, the characterization of biological factors and inhibitors to prevent the development of abnormal blood vessels in age-related macular degeneration. In glaucoma, there are opportunities for expanded research on the molecular mechanisms of fluid production and transport in the eye and on the cause of optic nerve damage; research to determine why the rate of glaucoma is higher and the disease possibly more severe in Blacks; the development of better noninvasive methods for evaluating optic nerve status; and, the development of new drugs and biologics to control intraocular pressure.

For diabetic retinopathy, the areas of greatest potential include research on the cell biology of the retina, including research on newly discovered growth factors which may play a role in the development of abnormal and destructive retinal blood vessels; the development of new drugs and molecular genetic techniques to inhibit aldose reductase activity (the enzyme which is involved in the pathogenesis of diabetic retinopathy); and, studies to understand how blood flow is regulated in the retina. In cataract research, potential rests in investigations of ways to augment the lens's natural defense mechanisms which prevent or retard cataract formation, in the conduct of molecular genetic studies to determine how the genetic expression of lens-specific proteins is regulated, and in biochemical studies to determine the critical changes in lens proteins that occur with age.

GLAUCOMA IN MINORITIES

Mr. Stokes: What are some of the findings of the Barbados Eye Study?

Dr. Kupfer: Data collection in the Barbados Eye Study is ongoing and will not be completed until April 1992. Preliminary findings of blindness and visual acuity impairment among 2,697 Black participants aged 40-84 have been reported. The prevalence of visual impairment, defined as best corrected visual acuity of <20/40 in the better eye, was 11.5%. The major cause of visual impairment was age-related cataract. The prevalence of blindness (best corrected visual acuity <=20/200 in the better eye) was 2.6%, and blindness most often resulted from cataract or glaucoma.

The causes of visual impairment and blindness are similar to those reported in an urban Black population surveyed in Baltimore. Prevalence rates of visual impairment and blindness are, however, double those found among urban Baltimore Blacks.

The Barbados Eye Study also has reported on factors associated with elevated intraocular pressure (IOP) in 2,676 Blacks. An IOP >=21mm Hg was present in 15.3% of Black participants and elevated intraocular pressures were associated with advancing age, high blood pressure, diabetes, large body size, and darker complexion.

CLINICAL TRIALS

Mr. Stokes: To what extent will clinical trials be conducted in FY 1993?

Dr. Kupfer: Ongoing clinical trials will be supported.

Mr. Stokes: To what extent will African Americans participate in these trials?

Dr. Kupfer: NEI-supported clinical trials have been very successful in securing the active participation of African Americans. They have been recruited in numbers which reflect the incidence or prevalence in African Americans of the specific condition being investigated. We expect this participation level to be sustained in FY 1993.

AGE-RELATED MACULAR DEGENERATION

Mr. Stokes: With the elderly population being one of the fastest growing, can we expect "AMD" to become an increasingly important national health problem?

Dr Kupfer: Yes, according to our best estimates, about 6.3 million older Americans will develop age-related macular degeneration (AMD) in the year 2030, compared to an estimated 1.7 million in 1995. AMD is an eye disease that destroys photoreceptor cells in the macula, the small specialized area of the central retina which is responsible for sharp, crisp vision. As the disease progresses, the acute vision that is needed for reading, driving a car, and other daily activities steadily diminishes.

Mr. Stokes: How do laser treatments affect "AMD?"

Dr. Kupfer: Laser treatment can prevent or postpone further loss of vision in some forms of AMD. However, the procedure does not restore vision already lost from macular degeneration. Moreover, at present, there is no proven way to either prevent AMD or to treat the vast majority of people who have the disease.

NUTRITION

Mr. Stokes: To what extent do vitamin C and vitamin E help to reduce the risk?

Dr. Kupfer: A clinical trial, the Age-Related Eye Disease Study (AREDS), will soon randomize individuals to high-dose antioxidant vitamins (beta-carotene, E, and C), zinc and copper. Approximately 4,600 participants will be followed for seven to eight years to determine the role of these nutrients on the development and progression of age-related macular degeneration (AMD) and cataract. The role of diet and blood nutrient levels in AMD is being examined in the AREDS and several other large population-based or case-control studies.

NATIONAL EYE HEALTH EDUCATION PROGRAM

Mr. Stokes: It is my understanding that the National Eye Health Education Program has had continued success in the development and implementation of program activities for persons at risk for glaucoma and diabetic eye disease. Tell us about this program.

Dr. Kupfer: The National Eye Health Education Program (NEHEP) is coordinated by the NEI in partnership with 40 public and private organizations. These groups, called the NEHEP Partnership, help to extend the reach of this national program into the local community. By working through their members and constituents, Partnership members plan and implement their own NEHEP-related eye health education programs targeted to a variety of high-risk audiences. The initial focus of the NEHEP is on public and professional eye health education emphasizing the importance of early detection and timely treatment of diabetic eye disease and open-angle glaucoma. In its first stage, the NEHEP is targeting its glaucoma public education messages to Blacks over age 40 and anyone over age 60. Because diabetes can occur at any age, and affects all racial and ethnic groups, the NEHEP is targeting its diabetic eye disease education program to all people with diabetes.

EYE HEALTH EDUCATION--ACCOMPLISHMENTS

Mr. Stokes: What have been some of the most significant accomplishments?

Dr. Kupfer: Significant accomplishments this year have included development of information and education strategies and materials for the glaucoma and diabetic eye disease programs; development of an applied research program for diabetic eye disease education; completion of a national survey of the public's knowledge, attitudes, and practices about eye health and disease, co-sponsored by the NEI and the Lions Clubs International; and the national launch of the Program.

NEHEP staff have developed strategies and materials designed to reach the target audiences through community, mass media, and interpersonal channels. Three kits have been developed: a Glaucoma Community Education kit, Educating People With Diabetes kit, and a Pharmacist Information kit. These kits include materials such as program guides, brochures, posters, prescription bag inserts, counter card displays, and a continuing education program for pharmacists.

For the glaucoma program, public service announcements (PSAs) were produced for television, radio, and print. The public service campaign was released in January 1992. To date, the TV PSAs are being aired in 47 states, by 203 stations, representing $1.8 million in air time. The radio PSAs are being aired in 49 states by 348 stations, representing $608,000 worth of air time.

For the diabetic eye disease applied research program, a request for grant applications for health education research in diabetic eye disease was issued in October 1991. We expect to make an award this fiscal year.

The NEHEP was formally launched in December 1991 at a national press conference hosted by Assistant Secretary for Health James O. Mason, M.D.. At that time, eye examination recommendations for individuals at risk for glaucoma and diabetic eye disease were released along with results from the national survey. Over 65 million people were exposed to this event through television, radio, newspapers, and magazines. New stories on the NEHEP continue to appear in the mass media.

EYE HEALTH EDUCATION--FUTURE PLANS

Mr. Stokes: What are your future plans for this program?

Dr. Kupfer: The NEHEP will be a continuing and evolving effort. In the future, the NEI will target additional eye diseases and eye health topics. However, for at least the next two years, the Program will focus only on diabetic eye disease and open-angle glaucoma, two of the most significant eye health problems in the United States for which effective therapies are available and early diagnosis provides the key to blindness prevention.

During the remainder of FY 92 and in FY 93, the NEI will work to increase the number of professional associations, voluntary and philanthropic organizations, corporations, state and Federal agencies, and civic groups that belong to the NEHEP Partnership. These partners provide additional opportunities to increase public awareness and further disseminate and leverage the NEHEP blindness prevention messages at both the national and local levels. In addition, the NEI will continue to provide technical expertise to Partnership members in the implementation and evaluation of community-based programs on glaucoma and diabetic eye disease.

The NEI will continue to address the special needs and concerns of minorities and other hard-to-reach audiences through the development of specific educational strategies and materials. The NEI will hold its third national eye health education conference in Spring 1993. The goal of this conference will be to enhance the health education and communication skills of organizations and individuals interested in eye health education.

It will also provide Partnership members the opportunity to share their experiences in implementing and evaluating effective eye health education programs.

EYE HEALTH EDUCATION--MINORITY NEEDS

Mr. Stokes: To what extent does the program address the special concerns and needs of minorities?

Dr. Kupfer: Glaucoma strikes African Americans at an earlier age and is often more severe than in other races. Epidemiologic studies have shown that Blacks have a 5 times greater risk for the disease than do Whites. In addition, the rate for blindness due to glaucoma is 6 times higher in Blacks than in the rest of the population. For these reasons, a primary goal of the NEHEP is to reach this high-risk population through a comprehensive multi-media campaign and community health education programs conducted through organizations and institutions that serve the Black community and older adults.

In addition, African Americans, Hispanics, and Native Americans are at an increased risk for diabetes and its complications. About 25 percent of African Americans over age 65 have diabetes, and evidence suggests that African Americans have a greater risk of developing diabetes-related complications. Mexican Americans have a threefold greater prevalence of non-insulin dependent diabetes mellitus (NIDDM) than non-Hispanic Whites. Diabetes has reached epidemic proportions among Native Americans, in some tribes the prevalence of diabetes is over 50 percent among older individuals. Therefore NEHEP educational strategies and materials are being developed to reach these specific minority groups at high risk for diabetes.

RESEARCH ACCOMPLISHMENTS

Mr. Early: What have been the most significant research accomplishments of the NEI?

Dr. Kupfer: Among the many accomplishments of the National Eye Institute, those that have had the greatest impact are related to the development of clinical trials to control the blinding diseases associated with diabetes. We now know that if laser treatment, that we have proved effective in treating diabetes retinopathy, is delivered in time, we can reduce by almost 98 percent the number of people with diabetes who will lose vision. That is a very impressive figure. Not only can we reduce blindness, but the dollars that have been saved by having this intervention available from the time the results of the study were published in 1976 to the present amount to as much as $1,200,000,000. I would say this has been a major step forward. The other accomplishments have been in the establishment of a research base in diseases of the retina, lens, and fluids of the eye that has yielded results that we have transferred to clinical trials, of new treatments for other eye diseases like glaucoma and eye diseases of newborns, such as retinopathy of prematurity.

OPPORTUNITIES ON THE HORIZON

Mr. Early: What are the major opportunities on the horizon in vision research?

Dr. Kupfer: There are many significant opportunities on the horizon in vision research. Included among them are:

Age-Related Macular Degeneration: AMD is an important and growing public health problem in older Americans. By 1995, it is estimated that 1.7 million Americans will have decreased vision from AMD, and the prevalence is expected to rise to 6.3 million by the year 2030, when an even greater percentage of our population enters its retirement years. Unfortunately, there is no proven way either to prevent macular degeneration or to treat the vast majority of people who have the disease. According to experts in the field, however, the scientific and technological capability now exists, with a greatly expanded effort, to make substantial progress against AMD. Some examples include: an expansion of basic research on the retina to identify genetic, nutritional, and age-related changes in the retina that contribute to the development of AMD; further exploration of retinal cell transplantation techniques; use of growth factors and other approaches for rescuing degenerating retinal cells; characterization of biological factors and inhibitors to prevent the development of abnormal blood vessels in AMD; and, launching new clinical trials to determine the effectiveness of vitamins, nutritional supplements, and minerals in preventing or treating AMD.

Glaucoma: The most common form of glaucoma is called open-angle glaucoma, a leading cause of blindness in the United States and the number one cause of blindness in Blacks. Approximately 3 million Americans have glaucoma, but about one-third are unaware of it. At present, glaucoma cannot be cured. According to experts in the field, the scientific and technological capability now exists, with a greatly expanded effort, to make substantial progress against glaucoma. Some examples include: basic research on the molecular mechanisms of fluid production and transport in the eye and on the cause of optic nerve damage in glaucoma; research to determine why the rate of glaucoma is higher and the disease possibly more severe in Black Americans; the development of better noninvasive methods for evaluating the health of the optic nerve; the development of new drugs and biologics to control intraocular pressure; and additional clinical trials of glaucoma treatments.

Diabetic Retinopathy: About one half of the Nation's estimated 14 million people with diabetes have at least early signs of diabetic retinopathy. According to experts in the field, the scientific and technological capability now exists, with a greatly expanded effort, to make substantial progress against diabetic retinopathy. Some examples include: an acceleration of research on the cell biology of the retina, including research on newly discovered growth factors which may play a role in the development of abnormal and destructive retinal blood vessels; the development of new drugs and molecular genetic techniques to inhibit aldose reductase activity, since accumulating experimental evidence indicates that this enzyme is involved in the pathogenesis of diabetic retinopathy; studies to understand how blood flow is regulated in the retina; and clinical investigations to assess risk factors for the severity and progression of diabetic retinopathy.

Cataract: Cataract is a major public health problem in this country, and is a leading cause of blindness in the world. At present, surgery to remove the opaque, non-functioning lens, followed by placement of a corrective contact or implanted lens is the only effective treatment for cataract. According to experts in the field, the scientific and technological capability now exists to make a greatly expanded effort to develop effective strategies to prevent or delay the formation of cataracts. Some examples include: investigations of ways to augment the lens's natural defense mechanisms, which prevent or retard cataract formation; conduct molecular genetic studies to determine how the genetic expression of lens-specific proteins is regulated and biochemical studies to determine the critical changes in lens proteins that occur with age; clinical studies to evaluate the safety and efficacy of anticataract drugs and methods of clinical management.

Mr. Early: To what extent will these opportunities be initiated in FY 1993?

Dr. Kupfer: The FY 1993 budget request provides real growth for investigator-initiated research project grants. To the extent that grant requests, for these funds, are in these areas then these opportunities will be initiated in FY 1993.

LONG-RANGE PLAN

Mr. Early: What is the status of the NEI program plan?

Dr. Kupfer: The National Eye Institute's (NEI) 5-year plan for vision research should be completed this Spring. For several months, our planning staff assisted in the development of the framework for developing an NIH Strategic Plan and provided input regarding accomplishments, needs, and opportunities related to eye and vision disorders to the various Trans-NIH Objectives panels. Development of the NEI Plan has resumed. Recently, as a further check on the NEI's Plan's credibility and relevance to the vision research community, drafts of the five disease-oriented Panel reports were mailed to recipients of NEI's MERIT award for review and comment. The response has been quite favorable with several constructive suggestions made for further improvement. Revised drafts will soon be sent as well to a group of reviewers in the optometric research community.

Mr. Early: Does your plan include the establishment of major research priorities, and if so, what are some of these priorities?

Dr. Kupfer: The new Plan does establish revised and new priorities for each of the NEI's 5 major programs. For the first time, these are stated in the form of key research questions to be addressed over the next 5 years. Some of these are:

- What are the molecular mechanisms of age-related macular degeneration? What is the role of genetics, nutrition, and systemic disease in the etiology of macular degeneration? What is the cause of cone cell dysfunction in age-related macular degeneration?

- What is the pathogenesis of diabetic retinopathy and other vascular diseases of the retina and choroid? What techniques or strategies will aid in preventing, diagnosing, and treating diabetic retinopathy? How does the anatomy, biochemistry, and physiology of the retina and choroidal vasculature differ in normal and diseased states? How is blood flow regulated in the retina?

- What developmental, biochemical, and biophysical factors determine the causes and mechanisms of cataract formation? What interventions can prevent or delay the developmental changes that lead to cataract? What are the factors that direct lens formation in the early embryo and are these factors related to known growth factors?

- What are the risk factors for glaucoma? Why are Black Americans at a greater risk for developing glaucoma at younger ages than other racial groups? What are the physiologic mechanisms of optic nerve damage due to glaucoma?

- How does the activity of individual neurons and groups of neurons relate to visual perception? How is visual information encoded by nerve cells and localized in centers of the brain?

- What techniques can be developed to measure the vision of infants and young children in order to study normal development and screen for and diagnose visual disorders?

- What is the nature of corneal inflammation and what methods can be developed to control it? What are the mechanisms of corneal wound healing?

AIDS

Mr. Early: What is the NEI doing in the AIDS research area?

Dr. Kupfer: The FY 1992 NEI budget for AIDS-related research is estimated at $5.9 million. Approximately 80% of this amount is devoted to research investigating various therapeutic agents to combat the various ocular complications of AIDS. The major activity in this regard has been the conduct of an extramural multicenter, randomized clinical trial to compare the safety and efficacy of two drugs--foscarnet and ganciclovir--for the initial treatment of CMV retinitis. Most of the remaining amount has been devoted to supporting laboratory investigations of the immunological mechanisms involved in producing the various AIDS-related "opportunistic" ocular infections.

Mr. Early: What are the future AIDS research priorities of the NEI?

Dr. Kupfer: The top NEI priority will remain the development of new therapeutic approaches to the treatment of the ocular complications of AIDS, and the testing of these treatments in rigorously conducted clinical trials.

Mr. Early: Are you supporting any AIDS-related research projects outside of the AIDS specific budget line?

Dr. Kupfer: We estimate that in FY 1992 approximately $500,000 outside of the AIDS specific budget line was provided to support AIDS-related research project grants. These are very-high-quality laboratory research projects which investigate fundamental questions related to the immunological mechanism which produce the "opportunistic" ocular complications of AIDS. These projects are also contributing to a better understanding of the special immunological properties of the normal visual system.

DIABETIC EYE DISEASE TREATMENT

Mr. Early: I understand that a new noninvasive technique has been developed to evaluate treatment of diabetic eye disease. Why is this advance considered important?

Dr. Kupfer: Blood flow changes in the retina have been documented in diabetic patients and in animal models of diabetes. A technique called laser doppler velocimetry (LDV) has been used to assess retinal blood flow in diabetic patients with different stages of diabetic retinopathy. Blood flow changes have been observed in patients with more advanced stages of retinopathy.

NEI intramural scientists, in collaboration with other NIH investigators have developed a noninvasive procedure for assessing aldose reductase activity in the lens, using nuclear magnetic resonance spectroscopy (NMR). This technique has potential for clinical application because it allows one to monitor the activity of this enzyme, which is implicated in producing some of the complications of diabetes, in the intact eye. Noninvasive techniques such as the LDV and NMR may provide information on the metabolic state of the retina and lens and serve as a tool for assessing treatment effectiveness.

NATIONAL EYE HEALTH EDUCATION PROGRAM--UPDATE

Mr. Early: Would you bring us up to date on the National Eye Health Education Program (NEHEP).

Dr. Kupfer: NEHEP accomplishments this year have included completion of a national survey of the public's knowledge, attitudes, and practices about eye health and disease; development of information and education strategies and materials for glaucoma and diabetic eye disease public education programs; and development of an applied research program for diabetic eye disease education.

The Second National Eye Health Education Conference was convened in February 1991. Participants were presented an overview of the latest scientific information and the elements of the proposed education and information activities. The Conference provided participants the opportunity to review materials and to make recommendations for the further development of the glaucoma and diabetic eye disease programs. In addition, participants described how their organizations will become involved in the implementation the NEHEP. Plans are now being developed for a third national conference to be convened in Spring 1993. This conference will give participants the opportunity to share experiences in the implementation and evaluation of eye health education projects including those designed to reach special populations. The NEHEP Partnership has been involved throughout the development of the program, and will participate in the program implementation, including dissemination of materials, co-sponsorship activities, and participation in applied research projects.

Following the conference, NEHEP staff developed strategies and materials designed to reach the NEHEP target audiences through community, mass media, and interpersonal channels. These include education kits; program guides, brochures and posters; public service announcements (PSAs) for television, radio, and print media; and a continuing education program for pharmacists. In November 1991, the pharmacy continuing education program on diabetic eye disease was published in a professional journal that reached 100,000 pharmacists. The public service campaign was released in January 1992.

The NEHEP was formally launched by Secretary of Health and Human Services Louis W. Sullivan at a national press conference in December 1991. At that time, eye examination recommendations for individuals at risk for glaucoma and diabetic eye disease were released as well as results from the national survey for people at risk for glaucoma. Extensive media coverage resulted from the press conference and NEHEP staff are counting on their efforts to publicize this national program.

Mr. Early: What are your plans for FY 92 and FY 93?

Dr. Kupfer: In the future, the NEI will target additional eye diseases and eye health topics. However, for at least the next two years, the Program will focus only on diabetic eye disease and open-angle glaucoma, two of the most significant eye health problems in the United States for which effective therapies are available and early diagnosis provides the key to blindness prevention.

During the remainder of FY 92 and in FY 93, the NEI will work to increase the number of professional associations, voluntary and philanthropic organizations, corporations, state and Federal agencies, and civic groups that belong to the NEHEP Partnership. These partners provide additional opportunities to increase public awareness and further disseminate and leverage the NEHEP blindness prevention messages at both the national and local levels. In addition, the NEI will continue to provide technical expertise to Partnership members in the implementation and evaluation of community-based programs on glaucoma and diabetic eye disease.

In FY 93, the NEI will continue to address the special needs and concerns of minorities and other hard-to-reach audiences through the development of specific educational strategies and materials. The NEI will hold its Third National Eye health Education conference in Spring 1993. The goal of this conference will be to enhance the health education and communication skills of organizations and individuals interested in eye health education. It will also provide Partnership members the opportunity to share their experiences in implementing and evaluating effective eye health education programs.

NATIONAL EYE HEALTH EDUCATION PROGRAM--ASSESSMENT

Mr. Early: What is your assessment of how well this program is working?

Dr. Kupfer: The extensive strategic planning that went into the development of the NEHEP has resulted in a Program that we are very proud of. This planning included extensive formative research and evaluation activities conducted prior to the production of the NEHEP materials, which contributed to their relevance and acceptability by the target audiences. Media coverage of the NEHEP launch and use of the public service announcements has been outstanding and has already increased public awareness of glaucoma and diabetic eye disease.

To support national efforts at the grassroots level, the NEHEP has established an effective network of organizations through the NEHEP Partnership. Each of these organizations has contributed to the development and implementation of the NEHEP, thus ensuring that communities work together to reach individuals at risk for glaucoma and diabetic eye disease. This level of cooperation is beginning to be experienced at the community level as local networks are being formed.

This combination of national and local programs working together helps to increase the likelihood that all Americans at risk will benefit from the progress made in the early detection and treatment of glaucoma and diabetic eye disease.

BIOTECHNOLOGY--VISION RESEARCH IMPACT

Mr. Early: What impact is biotechnology having on vision research?

Dr. Kupfer: Biotechnology is having an enormous impact on vision research. Biotechnology enables vision researchers to produce large amounts of biologically active substances at very low cost, permitting direct assay of these substances in the function of the visual system. Specific examples of studies made possible by the application of biotechnology include: determination of the role of growth factors, oncogenes, and extracellular matrix components on corneal wound healing; the pattern of collagen gene expression during corneal scar formation; the involvement of insulin-like growth factor in development of the ocular lens; the function of the $Na+/K+$ ATPase transporter in maintaining lens cytoskeleton structure; and the identification of point mutations in the ornithine aminotransferase gene responsible for gyrate atrophy of the choroid and retina.

RESEARCH TRAINING

Mr. Early: Support for research training awards, like that of all your other non-RPG extramural components of the budget, is frozen. What type of message do you think this sends to young people contemplating a career in biomedical research?

Dr. Kupfer: Funding increases for investigator-initiated research project grants have received the highest priority within the FY 1993 President's budget request. This will help to assure that monies are available when any newly-trained researchers are ready to apply for research projects. One must also keep in mind that many young people are employed as assistants on research grant projects, which often provides them a positive training experience.

Mr. Early: What impact might that message have on furthering advances in eye health care?

Dr. Kupfer: We continue to place a high priority on this activity, supporting a significant number of new investigators each year.

COOPERATIVE CLINICAL RESEARCH

Mr. Early: I notice your cooperative clinical research category is level. What is included under this area?

Dr. Kupfer: The FY 1993 request for the Cooperative Clinical Research category (in Other Research) is $25.6 million, unchanged from the FY 1992 Appropriation. Beginning in FY 1990, and with the Committee's encouragement, NEI consolidated in this category all its extramural support for clinical trials and other types of large-scale, fixed protocol clinical studies. These projects are all investigator-initiated, and most are funded as cooperative agreements in which members of the NEI extramural staff are involved substantial with the investigators. Our experience has been that this consolidation has greatly facilitated our clinical research planning and administrative efforts.

Mr. Early: Are these projects not as important as other investigator-initiated research projects?

Dr. Kupfer: These clinical trials and other applied clinical studies are important in carrying out NEI's mission, in translating new knowledge gained through biomedical research into advances in health care. However, the FY 1993 President's budget has placed a higher priority on funding increases for investigator-initiated research project grants.

Mr. Early: Are there any funds for new clinical trials in the Eye Institute 1993 budget request level?

Dr. Kupfer: No, the support provided in the fiscal year 1993 President's budget reflects funding for ongoing clinical trials.

CLINICAL TRIAL PLANNING GRANTS

Mr. Early: Doctor, bring us up to date on the Institute's Clinical Trials Planning Grants initiative. How many trials that have been developed with planning grants have been developed for implementation as full-scale clinical trials?

Dr. Kupfer: The National Eye Institute initiated the Clinical Trial Planning Grant program in August 1989 as a means of providing early peer review to investigators on the public health relevance of their proposed clinical trial and to evaluate the overall design features of the study. The Institute has received ten Clinical Trials Planning Grant applications which have been peer reviewed. Of these, five were recommended for consideration and were funded as Planning Grants between 1990 and 1992. Four of these five funded Planning Grants have resulted in the development of full-scale clinical trials that are currently awaiting peer review. If the peer reviews are favorable, it is possible the studies could be ready for implementation as early as FY 1993.

Mr. Early: Are funds included in your FY '93 request to continue this initiative?

Dr. Kupfer: We would expect to support this initiative at a level nearly equal to the current level of support.

CLINICAL TRIALS READY TO BE IMPLEMENTED

Mr. Early: Are there any clinical trials that could be undertaken in FY '93 if additional resources were available?

Dr. Kupfer: The FY 1993 President's budget includes $29.8 million for NEI clinical trials. Within these funds, NEI is supporting those projects which are considered to be among the highest priorities. If additional resources become available there are eleven other clinical trials that could be initiated in FY 1993.

Mr. Early: Would you give us some examples of those approved but unfunded trials which you consider to be a high priority?

Dr. Kupfer: The additional clinical trials which the Institute would like to support are in the following priority areas: glaucoma, AIDS, low-birthweight infants with eye complications, and corneal disease. Factors that influence the importance of these clinical trials are the public health importance of the problem, and the opportunities and technologies that are available to address the research questions.

Mr. Early: And, tell us why.

Dr. Kupfer: Factors that influence the priority of these clinical trials are the public health importance of the problem they address and the opportunities and technologies that are available to address the research questions. For example:

Glaucoma. This is the second leading cause of blindness in older Americans. The disease is more common in Blacks than Whites: approximately 5% of Blacks have glaucoma compared to 2% of Whites. Blacks tend to develop glaucoma at earlier ages and at lower ocular pressures compared to Whites. These findings indicate there may be a different point of intervention between Blacks and Whites.

AIDS. Cytomegalovirus (CMV) retinitis, a viral infection of the retina, the structure at the back of the eye that sends images to the brain, is a potentially blinding disease that affects about 20% of people with AIDS. Untreated, the disease leads to blindness. Results from an NEI-supported multicenter clinical trial showed that patients with AIDS with newly diagnosed CMV retinitis who were treated with foscarnet lived longer than those treated with ganciclovir. Both drugs were equally effective in halting the progression of the disease and preserving vision. Given the increasing number of people developing AIDS and the rapid developments in the area of drug treatment for AIDS-related diseases, there are opportunities for clinical trials to evaluate new drug treatments for CMV retinitis and new modes of drug delivery, as well as prophylaxis treatment for general CMV infections.

Low birthweight. For infants born under 1500 grams birthweight, approximately 2% are blinded by retinopathy of prematurity and another 5% have other permanent eye defects related to this eye disease. The incidence of retinopathy of prematurity increases with lower birthweight. Through the advances in medical technology, more premature, low birthweight infants are surviving which increases the number of infants at risk of developing this potentially blinding disease.

Corneal diseases. Corneal diseases, such as viral infections caused by herpes and a thinning and distortion of the cornea, result in severe impairment of vision. Treatments for preventing or reducing the effects of some of these diseases are ready for clinical evaluation.

CLINICAL TRIALS READY TO INITIATE

Mr. Early: Please provide for the record a list of these with a brief description of the trial, its duration, the first year cost and the estimated total cost of the trial.

Dr. Kupfer: A list of trials ready to initiate follows:

MAJOR NEW CLINICAL TRIALS READY TO BEGIN IF FUNDS WERE AVAILABLE

(Dollars in thousands)

	First Year	Total Projected
HERPETIC EYE DISEASES STUDY--II This study consists of two randomized, double-masked clinical trials and a study of risk factors for recurrence of ocular herpetic disease. The two randomized comparisons will be acyclovir vs. placebo for (1) the prevention or delay of herpetic recurrences and for (2) the prevention or delay of stromal keratitis or iritis subsequent to epithelial keratitis. Duration: 5 years	$1,800	$8,900
ADVANCED RETINOPATHY OF PREMATURITY STUDY The main objective of this multicenter, randomized clinical trial is to develop the best management strategy for children who fail cryotherapy. The study will assess the efficacy of scleral buckling surgery for Stage 4A and Stage 4B retinopathy of prematurity. Duration: 5 years	2,400	12,900
OCULAR HYPERTENSION STUDY The randomized clinical trial would determine whether lowering intraocular pressure by medical treatment (medications) prevents or delays the onset of glaucomatous optic disc and visual field damage in ocular hypertensive subjects who are judged to be at moderate risk for developing open-angle glaucoma. Duration: 9 years	3,200	26,100
STUDY OF INITIAL TREATMENTS FOR GLAUCOMA This randomized clinical trial would compare the efficacy of medication to filtration surgery as the initial therapy for newly diagnosed, open-angle glaucoma. Duration: 5 years	1,000	10,200

MAJOR NEW CLINICAL TRIALS READY TO BEGIN IF FUNDS WERE AVAILABLE
(Dollars in thousands)

	First Year	Total Projected
TREATMENT OF CMV RETINITIS IN PEOPLE WITH AIDS A prospective multicenter trial to compare alternative treatment strategies in management of patients experiencing relapse of CMV retinitis. Duration: 3 years	2,900	9,100
EFFECTS OF LIGHT REDUCTION ON RETINOPATHY OF PREMATURITY This proposed randomized clinical trial will examine whether reducing light to the eyes of prematurely born infants will prevent or reduce the incidence of moderate retinopathy of prematurity. Duration: 5 years	1,300	6,700
THERAPEUTIC OXYGEN IN RETINOPATHY OF PREMATURITY Premature infants who develop prethreshold retinopathy of prematurity will receive continuous transcutaneous oxygen saturation monitoring and be randomly assigned oxygen administration at one of two specified oxygen levels. Duration: 5 years	1,500	5,600
CONTACT LENS EVALUATION IN KERATOCONUS The proposed clinical trial will examine the effects of two different contact lens fitting methods for treating keratoconus: a flat fitting method where the contact lens touches the corneal apex, and a step fitting method where the contact lens clears the corneal apex. The trial would compare the safety and efficacy of the two fitting methods. Duration: 5 years	1,100	4,060
TREATMENT OF CONGENITAL ESOTROPIA This trial would consist of two phases: the first would establish preliminary data on the dosage of botulinum toxin, its effectiveness, and side effects; the second would consist of randomization of patients to treatment with botulinum toxin or to surgery for congenital esotropia. Duration: 5 years	2,200	8,700

MAJOR NEW CLINICAL TRIALS READY TO BEGIN IF FUNDS WERE AVAILABLE
(Dollars in thousands)

	First Year	Total Projected
PHASE III FOR CRYOTHERAPY FOR RETINOPATHY OF PREMATURITY Using the established cohort of children who have been treated with cryotherapy to prevent the progression of retinopathy of prematurity, the long-term visual outcome and anatomical features of the treated eyes will be assessed. Duration: 5 years	1,600	8,700
AREDS CLINICAL TRIAL A randomized, multicentered clinical trial to assess the effects of pharmacologic doses of (1) antioxidants and zinc on the progression of AMD and of (2) antioxidants on the development and progression of lens opacities. Duration: 8 years	4,000	39,000
Total, Clinical Trials	23,000	139,960

NIH FINANCIAL MANAGEMENT PLAN

Mr. Early: Doctor, what impact is the financial management plan having on your institute?

Dr. Kupfer: NEI supports the NIH Financial Management Plan and is committed to its implementation. Staff continues its long-standing practice of intensive grant-by grant budget reviews, and the NIH Core Principles have not required any major changes in NEI standard operating procedures.

CORE CENTER GRANTS

Mr. Early: Support for your Core Grant Awards is frozen at the FY 1992 level. What impact will this have on vision research?

Dr. Kupfer: The NIH request reflects its highest priorities--real growth--for research project grants, women's health, minority health, and maintaining the intramural program. To accomplish this, many other mechanisms have been straight lined. NEI Core Grants for Vision Research provide investigators who have achieved independent NEI funding with an additional support mechanism to: (1) enhance their institution's environment and capabilities for conducting vision research; (2) facilitate collaborative studies of the visual system and its disorders; and, (3) attract other scientists of diverse disciplines to research on the visual system. While the core grants have been straight-lined, fortunately the base support for these investigators, i.e., RPG's have real growth in FY 1993.

The number of NEI-supported Core Grants has remained stable since FY 1980, at approximately 30. However, in terms of constant dollars (BRDPI) the Core Grant budget category has lost more than 32 percent of its purchasing power since that time. The National Advisory Eye Council (NAEC) has reviewed both the number and the size of NEI-supported Core Grants. When considering the vastly increased new opportunities in vision research, the NAEC has concluded that there is a clear need to increase both the number and size of Core Grants. In the future, we would have to consider reductions in the number of RPG's to accomplish this if we conclude that core grants are a higher priority.

RESEARCH CENTERS--LEVEL OF SUPPORT

Mr. Early: Doctor, will NEI be able to fund noncompeting centers at commitment levels and competing centers at the peer reviewed levels under the budget request?

Dr. Kupfer: In fiscal year 1993, the adjustments for funding to core centers from the levels you described would be an estimated -17.2 percent.

RESEARCH PROJECT GRANTS--SUCCESS RATE

Mr. Early: What is the projected "success rate" for new and competing grants and how does this compare to the past two years?

Dr. Kupfer: For fiscal year 1993, the NEI's estimated success rate is 27 percent. This rate is 4 percentage points lower than the 1992 estimate of 31 percent, and 5.8 percentage points lower than the 1991 actual of 32.8 percent.

RESEARCH PROJECT GRANTS--PAYLINE PERCENTILE

Mr. Early: To what payline percentile will the Institute be able to fund under the budget request and how does this compare to FY 1992 and FY 1991?

Dr. Kupfer: For the NEI, the fiscal year 1993 budget request reflects a 31% payline percentile, compared to 34% for fiscal year 1992, and 36% for fiscal year 1991.

RESEARCH PROJECT GRANTS SUPPORT

Mr. Early: Will the Institute be able to fund noncompeting research project grants at commitment levels and new and competing research grants at the peer reviewed level?

Dr. Kupfer: The budget request reflects support of the noncompeting grants at the commitment level: on average, prior year cost will be increased by 4 percent for recurring costs, taking into account one-time, non-recurring costs such as equipment. For competing research project grants, the funding level contained in the budget request reflects on average an estimated -7.5 percent adjustment from the peer review recommended levels.

Mr. Early: What was the downward adjustment for noncompeting and competing grants in FY 1991 and FY 1992?

Dr. Kupfer: NEI is operating in concurrence with the NIH "Cost Management Plan" and support for research project grants reflects that policy. Noncompeting grants reflect funding sustained at the committed level, that is at the level of the prior year award plus a 4 percent inflation factor for recurring costs, taking into account one-time, non-recurring costs such as equipment. Under the Plan's policy, support for competing research projects reflects the prior year's average for competing grants plus the Biomedical Research and Development Price Index. For FY 1991, competing grants were adjusted on average 9.2% below the level recommended by the initial review group; noncompeting grants were adjusted on average 11.6% below recommended levels.

For FY 1992, competing grants are being adjusted an average 9.1% below the levels recommended by the initial review groups; noncompeting grants are being awarded at the commitment levels but approximately 11.6% below the levels originally recommended by the initial review groups. All grants are reviewed and funding needs are assessed on a case-by-case basis.

Mr. Early: What are you projecting for FY 1993?

Dr. Kupfer: For fiscal year 1993, the comparable adjustments would be about -10.3% for noncompeting and -7.5% for competing research project grants.

RESEARCH PROJECT GRANTS--OUT OF ORDER FUNDING

Mr. Early: Is the NEI making greater use of "out of order" funding to achieve a lower cost per award?

Dr. Kupfer: NEI's average grant costs continue to be relatively very low compared to other NIH funding components. NEI extramural program directors and grants management staff have always conducted an aggressive grant-by-grant review of all applications, both competing and non-competing, prior to award. Program relevance, portfolio balance, and other factors have always been taken into consideration in reaching funding decisions. While NEI has continued to consider cost as one such factor in making funding decisions, there has not been a need to make greater use of "out of order" funding based on cost considerations alone to reduce average grant costs.

STUDY SECTION RESPONSE

Mr. Early: How have NEI's study sections responded to limiting the average increase in the cost of a grant?

Dr. Kupfer: Most research project grant applications assigned to NEI are reviewed by study sections administered by the NIH Division of Research Grants. NEI's average grant costs have historically been among the lowest at the NIH. In part, this has been due to study section review of applications and to the intensive grant-by-grant review of costs conducted by NEI's extramural staff. We have not seen any major changes recently in study section behavior with regard to the review of those applications assigned to NEI. These groups continue to do a very good job of making broad budget recommendations.

Mr. Early: Have you detected any reluctance on the part of Councils and Boards to fund high risk research or young investigators?

Dr. Kupfer: On the contrary, the National Advisory Eye Council (NAEC) has been very supportive of the FIRST Award program and other programs to encourage new investigators. In addition, the NAEC has attempted to identify potential high-risk/high-payoff applications for special discussion and consideration. The NAEC strongly supports the continued, conservative, use of the MERIT award, because the longer length of these awards is believed to increase opportunities for high-risk, creative research.

RESEARCH PROJECT GRANTS--LENGTH OF AWARD

Mr. Early: Doctor, last year, if I recall correctly, you expressed some concern about shortening the length of a grant to four years. What effect has this had on your research programs?

Dr. Kupfer: There may be optimal lengths of grants in excess of four years for certain projects. Our challenge is to assure we support those projects where this is important. This requires balancing these against shorter award periods for other projects, both in NEI and elsewhere in NIH.

Mr. Early: Has the Institute experienced any particular difficulties?

Dr. Kupfer: The Institute is implementing this aspect of the NIH Financial Management Plan.

TRANSFER FUNDS FOR CANCER RESEARCH IN VISION

Mr. Early: For Fiscal 1992, the NEI will receive $1 million for cancer research from the National Cancer Institute. How do you plan to use these funds?

Dr. Kupfer: NEI will be able to pursue more aggressively a number of key opportunities for research which include: 1) identifying other possible genetic changes at the retinoblastoma (RB) gene locus that may be required for tumorigenicity, 2) determining the functional role of the RB gene in the normal embryological development of the retina, 3) delineating a possible role of oncogenes or anti-oncogenes in the etiology of ocular melanoma, and 4) developing new clinical approaches for managing RB and ocular melanoma.

SUPPORT FOR OTHER-RELATED RESEARCH

Mr. Early: In the category "Other Related Research," the number of awards decreases significantly. What types of activities does your institute support in this category, and does this decrease concern you?

Dr. Kupfer: The "Other Related Research" category for NEI includes support for Conference Grants (R13), Small Research Grants for Data Analyses (R03), Clinical Vision Research Development Awards (R21), Clinical Trial Planning Grants (R21), and the Small Instrumentation Grants Program (S15), and Scientific Review and Evaluation Awards. The numbers and dollars requested for FY 1993 are unchanged from the FY 1992 figures. If NEI is to take advantage of some of these opportunities, funding priorities must be set and adhered to. Other meritorious projects will go unfunded, and this is always a challenge. Within the FY 1993 budget request, we were able to provide real growth to our highest priority, i.e. research project grants.

USE OF ADDITIONAL FTEs

Mr. Early: The justification indicates that for both FY 92 and FY 93, you plan to increase the number of FTE's for both the intramural research program and research management and support. What are your plans?

Dr. Kupfer: The fiscal year 1993 budget request reflects authority for 255 FTEs, an increase of 8 over the fiscal year 1992 level of 247. We expect to distribute them as follows: 6 for the intramural and 2 for research management and support. Those in intramural would enable the Institute to capitalize on opportunities in gene therapy. Those in research management and support would be used to strengthen the National Eye Health Education Program and economic-cost benefit activities.

BUDGET COMPARISON

Mr. Early: What was NEI's professional judgement and how does it differ from the request before us?

Dr. Kupfer: The NEI's fiscal year 1993 professional judgement budget totals $359,553,000. There are programmatic and budget mechanism differences from the FY 1993 President's budget request. The professional judgement budget for example includes:

Program Differences:

+$25 million for age-related macular degeneration with an expansion of basic research on the retina to identify genetic, nutritional, or other age-related changes in the retina which contribute to the development of AMD; further exploration of transplantation techniques, use of growth factors, and other approaches for rescuing degenerating retinal cells; characterization of biological factors and inhibitors to prevent the development of abnormal blood vessels in AMD; and, launching new clinical trials to determine the effectiveness of vitamins, nutritional supplements, and minerals in preventing or treating AMD.

+$13 million in glaucoma for basic research on the molecular mechanisms of fluid production and transport in the eye and on the cause of optic nerve damage in glaucoma; research to determine why the rate of glaucoma is higher and the disease possibly more severe in Black Americans; the development of better noninvasive methods for evaluating the health of the optic nerve; the development of new drugs and biologics to control intraocular pressure; and additional clinical trials of glaucoma treatments.

+$10 million in diabetic retinopathy for an acceleration of research on the cell biology of the retina, including research on newly discovered growth factors which may play a role in the development of abnormal and destructive retinal blood vessels; the development of new drugs and molecular genetic techniques to inhibit aldose reductase activity, as accumulating experimental evidence indicates that this enzyme is involved in the pathogenesis of diabetic retinopathy; studies to understand how blood flow is regulated in the retina; and clinical investigations to assess risk factors for the severity and progression of diabetic retinopathy.

+$10 million for cataract to capitalize on the scientific and technological capability that now exists to make a greatly expanded effort to develop effective strategies to prevent or delay the formation of cataracts. Some examples include: investigations of ways to augment the lens's natural defense mechanisms, which prevent or retard cataract formation; conduct molecular genetic studies to determine how the genetic expression of lens-specific proteins is regulated; biochemical studies to determine the critical changes in lens proteins that occur with age; and clinical studies to evaluate the safety and efficacy of anticataract drugs and methods of clinical management.

By Program:

	Fiscal Year 1993 (Dollars in thousands)	
Activity:	Request Level	Professional Judgement
Vision Research		
Extramural	$242,585	$306,216
Intramural Research	30,705	30,705
Extramural Construction	--	10,000
Research Mgmt. & Support	11,843	12,632
Total, NEI	285,133	359,553

Budget Mechanism Differences:

Compared to the 1993 request level, under the professional judgement budget, support for research project grants and core center grants would reflect full funding and the number supported would increase; a 50 percent success rate would be supported for competing research project grants; new clinical trials would be initiated; support for research careers and research training would be strengthened significantly; research and development contracts effort would be expanded; and support would also be provided for extramural construction awards:

Mechanisms:	Fiscal Year 1993 (Dollars in thousands) Request Level No.	Request Level Amount	Profess. Judge. No.	Profess. Judge. Amount
Research project grants	1,009	$193,274	1,203	$230,953
Core grants	30	7,655	36	12,597
Other Research	220	29,180	300	44,212
Research Training	262	7,294	289	8,454
R&D Contracts		5,182		10,000
Extramural Construction		--		10,000
Intramural Research		30,705		30,705
Res. Mgmt. & Supp.		11,843		12,632
Total, NEI		285,133		359,553

DELAYED OPPORTUNITIES

Mr. Early: Will any significant new research initiatives or opportunities be lost or delayed by lack of funds in the FY 1993 budget request?

Dr. Kupfer: There are always more scientific opportunities to pursue than resources to support them. Within the funds available, NEI is supporting those projects which it believes are the highest priority. If additional resources become available, NEI would not need to delay work on opportunities that are ready to be exploited to further improvements in eye health care and the quality-of-life. There are significant quality of life benefits to be had from further basic and clinical vision research including cataract, glaucoma, diabetic eye disease, and age-related macular degeneration.

OPPORTUNITIES READY TO EXPLOIT

Mr. Early: What priorities would the Institute pursue if additional resources were available?

Dr. Kupfer: If added resources were available, the NEI would pursue accelerated and expanded basic and clinical research in a number of areas in vision research that are ready for exploitation including glaucoma, cataract, macular degeneration, and diabetic eye disease to name a few.

Mr. Early: If an increase over the FY 1993 request is provided, how would you use these additional funds?

Dr. Kupfer: In my professional judgement, if additional funds were made available in fiscal year 1993, the NEI would capitalize on the many opportunities now at hand for improving the quality-of-life for the millions of Americans that suffer from such eye diseases and vision impairments.

Extent of the vision problem:

Age-Related Macular Degeneration: AMD is an important and growing public health problem in older Americans. By 1995, it is estimated that 1.7 million Americans will have decreased vision from AMD, the prevalence is expected to rise to 6.3 million by the year 2030, when an even greater percentage of our population enters its retirement years. Unfortunately, there is no proven way to either prevent macular degeneration or to treat the vast majority of people who have the disease.

Glaucoma: The most common form of glaucoma is called open-angle glaucoma, a leading cause of blindness in the United States and the number one cause of blindness in Blacks. Approximately 3 million Americans have glaucoma - but about one-third are unaware of it. At present, glaucoma cannot be cured.

Diabetic Retinopathy: About one half of the Nation's estimated 14 million people with diabetes have at least early signs of diabetic retinopathy.

Cataract is a major public health problem in this country, and is a leading cause of blindness in the world. At present, surgery to remove the opaque, non-functioning lens, followed by placement of a corrective contact or implanted lens is the only effective treatment for cataract.

Research effort required:

According to experts in the field, the scientific and technological capability now exists, with a greatly expanded effort, to make substantial progress against these eye diseases and impairment through: expansion of basic research on the retina to identify genetic, nutritional, or other age-related changes in the retina which contribute to the development of AMD;

o further exploration of transplantation techniques, use of growth factors, and other approaches for rescuing degenerating retinal cells;

o characterization of biological factors and inhibitors to prevent the development of abnormal blood vessels in AMD and, launching new clinical trials to determine the effectiveness of vitamins, nutritional supplements, and minerals in preventing or treating AMD;

o basic research on the molecular mechanisms of fluid production and transport in the eye and on the cause of optic nerve damage in glaucoma;

o research to determine why the rate of glaucoma is higher and the disease possibly more severe in Black Americans and development of better noninvasive methods for evaluating the health of the optic nerve;

o development of new drugs and biologics to control intraocular pressure and conduct of additional clinical trials of glaucoma treatments;

o acceleration of research on the cell biology of the retina, including research on newly discovered growth factors which may play a role in the development of abnormal and destructive retinal blood vessels;

o development of new drugs and molecular genetic techniques to inhibit aldose reductase activity, as accumulating experimental evidence indicates that this enzyme is involved in the pathogenesis of diabetic retinopathy;

o studies to understand how blood flow is regulated in the retina and clinical investigations to assess risk factors for the severity and progression of diabetic retinopathy;

o investigations of ways to augment the lens's natural defense mechanisms, which prevent or retard cataract formation;

o molecular genetic studies to determine how the genetic expression of lens-specific proteins is regulated and biochemical studies to determine the critical changes in lens proteins that occur with age; and

o clinical studies to evaluate the safety and efficacy of anticataract drugs and methods of clinical management.

CAUSES OF BLINDNESS

Mr. Pursell: What are the leading causes of blindness in the United States?

Dr. Kupfer: The leading causes of blindness and visual disability are aging-related maculopathy, cataract, glaucoma, diabetic retinopathy, and optic nerve atrophy.

COST OF BLINDNESS

Mr. Pursell: Are there any estimates of federal budgetary costs associated with blindness?

Dr. Kupfer: Age-related macular degeneration (AMD) is an important and growing public health problem in older Americans. By 1995, it is estimated that 1.7 million Americans will have decreased vision from AMD, and 100,000 will be blind from the disease. The prevalence of AMD is expected to rise to 6.3 million by the year 2030, when an even greater percentage of our population enters its retirement years. Blindness from glaucoma costs the U.S. government more than $1.5 billion annually in Social Security benefits, lost tax revenues, and health care expenditures. It is estimated that blindness from diabetic retinopathy costs the U.S. government approximately $13,607 annually per person affected in Social Security benefits, lost tax revenue, and health care expenditures. This amounts to a total of approximately $1.1 billion annually. In the U.S., cataract surgery is the most frequently performed operation among people over age 60. Approximately 1.5 million cataract operations are performed annually, at a total cost exceeding $5 billion. Reimbursement for cataract surgery now accounts for 12 percent of the entire Medicare budget.

DIABETIC RETINOPATHY CLINICAL TRIAL

Mr. Pursell: What are the projected cost savings of the diabetic retinopathy clinical trial?

Dr. Kupfer: The Diabetic Retinopathy Study initiated in 1976 at a total cost of less than $11,000,000 has yielded savings in excess of $1,200,000,000 in terms of decreasing blindness from this disease.

Mr. Pursell: How are the results of the diabetic retinopathy trials being translated into direct patient care?

Dr. Kupfer: This is being done aggressively in various ways. From the time the findings of our original clinical trial--which was the first to demonstrate conclusively the value of laser treatment in preventing severe visual loss from diabetic retinopathy--were announced in 1976, the NEI and other organizations and individuals have taken a very active role in encouraging the incorporation of this information into patient care.

In 1976 and every time thereafter when our trials have achieved clinically important results, the NEI has launched an extensive informational effort, directed at eye care professionals as well as people with diabetes and their families. This effort has included, among other techniques, direct mail to health professionals indicating how the studies' results may be translated to patient care; use of the mass media; exhibits at medical meetings; educational audiovisual materials; articles in ophthalmologic, optometric, and allied health newsmagazines; and incorporation of questions testing knowledge of the trial results into ophthalmology board examinations. In addition, the Centers for Disease Control, through its state-based diabetes translation program, has strongly promoted the application of these results, particularly through its very widely read and followed physician's guide to the treatment of diabetic complications.

Other major efforts have been made by the American Academy of Ophthalmology, American Optometric Association, American Diabetes Association, and Juvenile Diabetes Association to educate their members and supporters about the importance of early detection of diabetic eye disease so that sight-saving treatment can be applied at the appropriate time. Recently the ophthalmology academy has launched Diabetes 2000, a large-scale national educational effort, primarily aimed at internists and other primary care physicians, concerning the importance of eye exams for their diabetic patients and the value of timely treatment.

Finally, the NEI has launched the National Eye Health Education Program (NEHEP), a Congressionally mandated program, that is a full-scale national educational effort targeting people with diabetes--with messages about the importance of having regular eye examinations through dilated pupils. In carrying out this effort, the NEHEP is making use of a wide variety of media and channels. Most importantly, NEHEP has been formally joined in its efforts by over 40 public and private sector organizations, including those mentioned above, who will considerably multiply the impact of this program.

Much has already been done to translate this vital information into direct patient care and, to a large degree, these efforts have been highly successful. Yet, studies have also shown that there is much left to do: too many people with diabetes are still not having the necessary periodic professional eye examinations and/or not complying with recommendations for treatment. Also, many physicians are not routinely referring their patients for diabetic eye care. We have done much, but there is much more to do. We are highly optimistic that NEHEP and other national programs concerned with preventing blindness from diabetic retinopathy will effectively bridge these remaining gaps in the translation of these clinical trial results.

DIABETIC RETINOPATHY RESEARCH

Mr. Pursell: Would you please provide an overview for the Subcommittee of the NEI-sponsored research that is being conducted in an effort to prevent diabetic retinopathy.

Dr. Kupfer: Diabetic retinopathy is the leading cause of blindness in adults under age 65 and accounts for approximately 12 percent of the new causes of blindness each year in the United

States. About half of the Nation's estimated 14 million people with diabetes have early signs of this disease. Vision loss is a consequence of abnormal growth of blood vessels on the retina, the light sensitive tissue at the back of the eye. Basic and clinical investigations are being conducted in an effort to improve the prevention, detection, and treatment of diabetic retinopathy for millions of Americans.

Some examples include: in the area of cell biology, the identification and characterization of growth factors that may play a role in the proliferation of abnormal and destructive blood vessels in the retina; the development of new strategies for the inhibition of aldose reductase, an enzyme that may be involved in the pathogenesis of diabetic retinopathy; and development of noninvasive procedures for assessing aldose reductase in the eye. In clinical research, a population-based epidemiologic study of the four-year incidence and progression of diabetic retinopathy is providing needed information regarding eye health care needs of those with diabetes, emphasizing the need for control of hypertension.

In addition, the NEI has been coordinating the National Eye Health Education Program, which at present is targeted at individuals and groups at high risk for glaucoma and diabetic eye disease. Information and education strategies for targeting audiences with diabetic retinopathy is underway.

ALDOSE REDUCTASE INHIBITORS

Mr. Pursell: What are aldose reductase inhibitors?

Dr. Kupfer: Diabetic retinopathy, one of the most important causes of visual loss, is an eye disease that may develop in people with diabetes. Abnormal new blood vessels grow on the surface of the retina and cause loss of vision. Research now indicates that aldose reductase, found in many retinal cells and the principal enzyme by which sugars such as glucose and galactose are converted to sugar alcohols, is involved in the pathogenesis of diabetic retinopathy. Aldose reductase inhibitors have the potential to inactivate aldose reductase and prevent the damaging effect of these sugar alcohols. Therefore, the inhibition of aldose reductase by both new drugs and molecular genetic techniques is a promising area of research in preventing or slowing the progression of diabetic retinopathy.

OPPORTUNITIES IN DIABETIC RETINOPATHY

Mr. Pursell: Are there any research opportunities in diabetic retinopathy that could be expanded upon or initiated in FY '93 if new money were available?

Dr. Kupfer: The FY 1993 President's budget includes $20 million for research on diabetic eye disease. Within those available funds, NEI is supporting those projects which it believes are among the highest priority in this field. According to experts in the field, the scientific and technological capability now exists, with a greatly expanded effort, to make substantial progress against diabetic retinopathy. Some examples include: an acceleration of research on the cell biology of the retina, including research on newly discovered growth factors which may play a role in the development of abnormal and destructive retinal blood vessels; the development of new drugs and molecular genetic techniques to inhibit aldose reductase activity, as accumulating experimental evidence indicates that this enzyme is involved in the pathogenesis of diabetic retinopathy; studies to understand how blood flow is regulated in the retina; and clinical investigations to assess risk factors for the severity and progression of diabetic retinopathy.

Mr. Pursell: How much would it cost to support those initiatives?

Dr. Kupfer: In my professional judgement, support to capitalize on these opportunities in diabetic eye disease would cost $10 millions in new monies.

EYE DISEASES PREVALENT IN THE ELDERLY

Mr. Pursell: Are certain types of eye disease particularly prevalent in the elderly population?

Dr. Kupfer: Many diseases of the eye and brain visual pathway that result in blindness or reduced vision are directly related to aging. Diseases and disorders such as cataract, glaucoma, and age-related macular degeneration are leading causes of blindness and visual impairment among older Americans. With older people making up the fastest growing part of the U.S. population, age-related eye disorders will become even more important in the coming decades.

EYE DISEASE AND NUTRITION RELATIONSHIP

Mr. Pursell: Is there a relationship between these diseases and nutrition?

Dr. Kupfer: An NEI-initiated study to learn more about the possible role of nutrition in the development and progression of AMD and cataract, the Age-Related Eye Diseases Study (AREDS) will include more than 4,600 volunteers throughout the Nation and will be the first large-scale attempt to follow the clinical course of these two eye diseases. Nutrition supplements and minerals will be evaluated in a randomized clinical trial. Recent animal and case-control studies have suggested a protective effect of antioxidant nutrients such as vitamins C, E, and b-carotene against the development of cataract and age-related macular degeneration (AMD). A small, inconclusive clinical trial reported that zinc retards the progression of AMD.

NIH PRIORITIES IN AGING RESEARCH

Mr. Pursell: Please outline the NEI-sponsored research included in the aging priorities of the NIH's framework for discussion.

Dr. Kupfer: The NEI has identified a number of research priorities related to aging, as the result of its own strategic planning process and in conjunction with the development of the NIH Framework for Discussion. The priorities listed below include research on age-related macular degeneration, age-related cataract, glaucoma, and rehabilitation of the visual impairment that results from these and other eye diseases and visual disorders.

Age-related macular degeneration (AMD). The NEI is strongly committed to research that will:

- increase understanding of the biology of macular function and pathology of age-related macular degeneration;
- investigate the cause of retinal cell dysfunction in AMD; and
- identify specific retinal epithelium cell genes that may be involved in the etiology of AMD.

Age-related cataract. NEI's priorities for cataract research include:

- biochemical characterization of cataractogenesis;
- development of interventions that can prevent or delay cataract formation;
- determination of how changes in protein sequence and structure affect lens transparency; and
- investigation of whether there are unique aspects of aging in the lens or whether information derived from other studies of aging can be applied to cataracts.

Glaucoma. The NEI's glaucoma research priorities include studies that will:

- identify the cellular and molecular basis of the function of the ciliary body, which secretes aqueous humor, and the trabecular meshwork, the tissue through which aqueous humor filters from the eye, so that pathological mechanisms in glaucoma can be better understood;
- determine the physiologic mechanisms of optic nerve damage so that therapy can be designed to decrease the risk of vision loss from glaucoma;
- develop clinically relevant and reproducible diagnostic criteria for glaucoma and its progression;
- identify risk factors for glaucoma; and
- develop newer and more effective treatments.

Visual Impairment and its Rehabilitation. The NEI's priorities include:

- developing standardized tests to provide a profile of visual capacities and their relationship to common clinical measures of vision;
- investigating interactions between visual, cognitive, motivational, and other physical limitations to performance; and
- developing new devices for visually impaired individuals such as ergonomically designed magnifiers, telescopic spectacles, and voice control and output for computers.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

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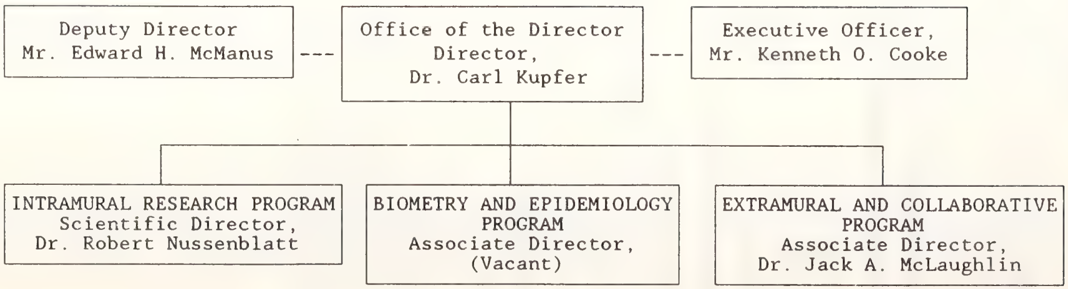
NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Organization Structure



NATIONAL INSTITUTES OF HEALTH

National Eye Institute

For carrying out section 301 and title IV of the Public Health Service Act with respect to eye diseases and visual disorders, [$271,002,000] *$285,133,000*: *Provided*, That of the funds made available under this heading, [$12,504,000] *$14,974,000* shall not become available for obligation until September 30, [1992] *1993*.

(Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 1992.)

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JUSTIFICATION OF THE BUDGET ESTIMATES

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Amounts Available for Obligation[1]

	1991 Actual	1992 Appropriation	1993 Estimate
Appropriation............	$260,159,000	$271,002,000	$285,133,000
Sequester order..........	-3,000	---	---
Section 514 (a) reduction	-648,000	---	---
Section 514 (b) reduction	-6,270,000	---	---
Section 214 travel reduction...............	---	-69,000	---
Section 513 (a) travel reduction...............	---	-112,000	---
Section 513 (a) S&E reduction...............	---	-1,521,000	---
Subtotal, adjusted appropriation.........	253,238,000	269,300,000	285,133,000
Real transfer from other accounts for the Shannon awards..........	207,000	---	---
Real transfer from the National Cancer Institute for cancer research.........		1,000,000	---
Subtotal, adjusted budget authority......	253,445,000	270,300,000	285,133,000
Unobligated balance lapsing.................	-91,000	---	---
Total obligations........	253,354,000	270,300,000	285,133,000

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[1] Excludes the following amounts for reimbursements activities carried out under this account: 1991 - $754,000; 1992 - $315,000; and 1993 - $115,000.

NATIONAL INSTITUTE OF HEALTH

National Eye Institute

Budget Mechanism
(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	No.	Amount	No.	Amount	No.	Amount
Research grants:						
Research projects						
Noncompeting	770	$127,876	758	$134,861	778	$148,683
Admin. supplemental	(31)	1,628	(18)	440	(18)	456
Competing						
Renewals	128	25,907	128	23,318	120	22,927
New	119	16,601	120	21,860	111	21,208
Supplemental						
Subtotal, competing	247	42,508	248	45,178	231	44,135
Subtotal, research projects	1,017	172,012	1,006	180,479	1,009	193,274
Research centers						
Core/specialized	30	7,361	30	7,655	30	7,655
Other research						
Research career prog.	22	1,709	20	1,616	20	1,616
Cooperative clin. res.	139	20,670	160	25,638	160	25,638
Biomedical research support						
Minority biomedical support		236		335		335
Other res. related	69	2,857	40	1,591	40	1,591
Subtotal, other res.	230	25,472	220	29,180	220	29,180
Total, research grants	1,277	204,845	1,256	217,314	1,259	230,109

Training:						
Individual awards						
Noncompeting..........	50	1,353	44	1,165	59	1,544
Competing.............	45	1,078	41	1,060	26	681
Subtotal, individual awards..............	95	2,431	85	2,225	85	2,225
Institutional awards						
Noncompeting..........	114	3,402	147	4,304	138	4,002
Competing						
Renewal..............	11	291	20	510	28	766
New..................	41	1,170	10	255	11	301
Subtl, institutional.........	166	4,863	177	5,069	177	5,069
Total, training.........	261	7,294	262	7,294	262	7,294
Research & development contracts.............	18	4,953	51	5,182	51	5,182
	FTEs		FTEs		FTEs	
Intramural research.....	164	26,532	174	29,220	180	30,705
Research management and support...............	65	9,821	73	11,290	75	11,843
Extramural construction						
TOTAL..................	229	253,445	247	270,300	255	285,133
Clinical Trials........		(24,244)		(29,904)		(29,836)

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Crosswalk - 1991 Actual

(Dollars in thousands)

Program Activity	Mechanism								
	Research Grants			Training Programs		Research & Development Contracts	Intramural Research	Research Management & Support	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional				
Vision research	$172,012	$7,361	$25,472	$2,431	$4,863	$4,953			$217,092
Intramural research							$26,532		$26,532
Research management and support								$9,821	$9,821
Total	172,012	7,361	25,472	2,431	4,863	4,953	26,532	9,821	253,445

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Crosswalk - 1992 Appropriation

(Dollars in thousands)

Program Activity	Mechanism								
	Research Grants			Training Programs					
	Research Projects	Research Centers	Other Research	Individual	Institutional	Research & Development Contracts	Intramural Research	Research Management & Support	Total
Vision research	$180,479	$7,655	$29,180	$2,225	$5,069	$5,182			$229,790
Intramural research							$29,220		29,220
Research management and support								$11,290	11,290
Total	180,479	7,655	29,180	2,225	5,069	5,182	29,220	11,290	270,300

NATIONATIONAL INSTITUTES OF HEALTH

National Eye Institute

Crosswalk - 1993 Estimate

(Dollars in thousands)

Program Activity	Mechanism								
	Research Grants			Training Programs		Research & Development Contracts	Intramural Research	Research Management & Support	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional				
Vision research	$193,274	$7,655	$29,180	$2,225	$5,069	$5,182			$242,585
Intramural research							$30,705		30,705
Research management and support								$11,843	11,843
Extramural construction ...									
Total	193,274	7,655	29,180	2,225	5,069	5,182	30,705	11,843	285,133

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Summary of Changes

1992	Estimated budget authority	$270,300,000
1993	Estimated budget authority	285,133,000
	Net change	+ 14,833,000

	1992 Current Estimate Base: Pos. (FTE)	1992 Current Estimate Base: Budget Authority	Change from Base: Pos. (FTE)	Change from Base: Budget Authority
Changes:				
A. Built-in:				
1. Within grade increase		$13,905,000		+$113,000
2. Annulization of January 1992 pay raise		13,905,000		+146,000
3. One less day of pay		13,905,000		-49,000
4. January 1993 pay raise		13,905,000		+386,000
5. Payment for management fund services		10,701,000		+662,000
6. Service and supply fund increase		2,784,000		+103,000
7. Increased costs of supplies, materials and services		15,904,000		+537,000
8. DHHS Working Capital Fund		353,000		+19,000
Subtotal				1,917,000
B. Program:				
1. Research projects grants:	No.	Amount	No.	Amount
a. Noncompeting	758	135,301,000	+20	+13,838,000
b. Competing	248	45,178,000	-17	-1,043,000
Total	1,006	180,479,000	+3	+12,795,000
	Pos. (FTE)	Budget Authority	Pos. (FTE)	Budget Authority
2. Intramural research program	(174)	29,220,000	(+6)	+59,000
3. Research management and support program activities	(73)	11,290,000	(+2)	+62,000
Subtotal				+12,916,000
Total changes			(+8)	+14,833,000

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Budget Authority by Activity
(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	FTE	Amount	FTE	Amount	FTE	Amount
Vision research	---	$217,027	---	$229,790	---	$242,585
Intramural research	164	26,506	174	29,220	180	30,705
Research management and support	65	9,821	73	11,290	75	11,843
Total obligations	229	253,354	247	270,300	255	285,133
Unobligated balance lapsing		+91		---		---
Total, budget authority	229	253,445	247	270,300	255	285,133
HIV/AIDS	(9)	(5,680)	(9)	(5,902)	(9)	(6,221)

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Budget Authority by Object

	1992 Appropriation	1993 Estimate	Increase or Decrease
Number of full-time permanent positions.......	180	185	+5
Total compensable workyears:			
Full-time equivalent employment.....	254	262	+8
Full-time equivalent of overtime and holiday hours...	1	1	--
Average ES salary..	$103,947	$107,793	+$3,846
Average GM/GS grade.	10.43	10.43	--
Average GM/GS salary	$41,741	$43,286	+$1,545
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)....	$66,824	$69,296	+$2,472
Average salary of ungraded positions	$25,683	$26,633	+$950
Personnel compensation:			
Permanent positions	$7,561,000	$7,888,000	+$327,000
Positions other than permanent........	3,134,000	3,268,000	+134,000
Other personnel compensation.....	348,000	363,000	+15,000
Special personnel services.........	883,000	918,000	+35,000
Total personnel compensation.....	11,926,000	12,437,000	+511,000

	1992 Appropriation	1993 Estimate	Increase or Decrease
Personnel benefits..	$1,979,000	$2,064,000	+85,000
Travel and transportation of persons............	321,000	443,000	+122,000
Transportation of things............	82,000	82,000	--
Rent, communications, and utilities......	430,000	445,000	+15,000
Printing and reproduction.......	190,000	199,000	+9,000
Other services:			
Project contracts..	5,182,000	5,182,000	--
Centrally furnished services..........	10,701,000	11,446,000	+745,000
Other..............	10,424,000	10,893,000	+469,000
Supplies and materials	2,492,000	2,501,000	+9,000
Equipment...........	1,965,000	2,038,000	+73,000
Grants, subsidies and contributions......	224,608,000	237,403,000	+12,795,000
Total, budget authority........	270,300,000	285,133,000	+14,833,000

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Significant Item in the Senate Appropriations Committee Report

Support to Schools of Optometry and Optometrists' Participation in Institute Activities

The Senate report 102-104, page 122 stated "...... the Committee most strongly urges NEI to utilize the expertise of qualified optometrists and, further, to provide the Committee with a report regarding the extent to which grants have been provided to optometry schools within the past 3 years."

Action Taken or to be Taken - The NEI conducted an analysis of these two areas. Results for the fiscal year 1989-1991 period revealed the following summary. The percentage of competing research project grant applications submitted by schools, colleges, and departments of optometry, and persons with the Doctor of Optometry Degree equals their percent of competing grants funded (4.2 percent). Success rate for this category of grantees is about equal to the NEI average, both of which exceed the NIH average. (Averaged for the fiscal year 1989-1991 period, schools and colleges 37.5 percent, research optometrists not at schools of optometry 39.2 percent [FY'91 was 50%], NEI total 37.6 percent, estimated NIH total about 26 percent.)

Optometrists are active participants in NEI committees, panels, review groups, and workshops: Involved in the development of NEI's long range plan; partner in NEI's National Eye Health Education Program (and represented on the NEHEP planning committee); and represented on the National Advisory Eye Council. (DHHS' appointment of members to the upcoming council term is underway.) They are involved in NEI clinical research activities; and participate in scientific review committees. The detailed report has been forwarded to the Committee.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Authorizing Legislation

	PHS Act/Other Citation	U.S. Code Citation	1992 Amount Authorized	1992 Estimate	1993 Amount Authorized	1993 Budget Request
Research and Investigation..	Section 301	42§241	Indefinite	$263,006,000	Indefinite	$277,839,000
National Eye Institute......	Section 455	42§851	Indefinite		Indefinite	
National Research Service Awards.	Section 487(d)	42§288	Authorizing legislation is pending 1/	7,294,000	Authorizing legislation is pending 1/	7,294,000
Total, Budget Authority......				270,300,000		285,133,000

1/ This training authority is shared with other research training programs of the National Institutes of Health, and the Alcohol, Drug Abuse, and Mental Health Administration.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Appropriation History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation[1]
1983	$131,550,000	$138,763,000	$145,040,000	$141,897,000
1984	142,333,000	149,600,000 2/	151,966,000 2/	152,262,000
1985	157,873,000	272,097,000 3/	187,181,000	178,591,000
1986	183,341,000	188,988,000 4/	184,036,000	195,094,000
1986 Sequester				-8,389,000
1987 5/	179,201,000	219,091,000	214,080,000	216,637,000
1988	184,829,000	234,382,000 6/	231,529,000	224,947,000
1989	229,021,000 7/	223,288,000 8/	229,271,000	234,218,000
1990	223,777,000 9/	240,636,000	241,774,000	239,889,000 10/
1990 Sequester				-3,356,000
1991	247,392,000	254,887,000 11/	258,324,000	253,241,000 12/
1991 Sequester				-3,000
1992	272,260,000	272,260,000	267,229,000	269,300,000 13/
1993	285,133,000			

[1] Reflects enacted supplementals, rescissions, and reappropriations.

[2] Excludes $3,585,000 in NRSA training programs not considered.

[3] Excludes $3,900,000 in NRSA training programs not considered.

[4] Excludes $5,231,000 in NRSA training programs not considered.

[5] The budget estimate to congress proposed that all funding for AIDS research be consolidated in the Office of the Assistant Secretary for Health. The House allowance consolidated all NIH AIDS funding in the Office of the Director; NIH: the Senate allowance and the appropriation spread the funding among the Institutes, including $104,000 for the NEI.

[6] Does not include funding for AIDS research consolidated at the Secretary's level.

[7] The 1989 request excludes funds for AIDS research and education ($4,947,000) proposed for consolidation in the Office of the Assistant Secretary for Health.

[8] Excludes $5,620,000 in NRSA training programs not considered.

[9] The 1990 request excludes funds for AIDS research and education ($5,697,000) proposed for consolidation in the Office of the Assistant Secretary for Health.

[10] Excludes enacted administrative reductions of $1,316,000.

[11] Excludes $7,105,000 in NRSA training programs not considered.

[12] Excludes enacted administrative reductions of $6,918,000.

[13] Reflects enacted administrative reductions totaling $1,702,000.

Justification

National Eye Institute

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
229	$253,445,000	247	$270,300,000	255	$285,133,000	+8	+$14,833,000

General Statement

Eye diseases and vision disorders affect the lives of millions of people worldwide. More than ten million Americans have irreversible impairment from visual disorders and about 900,000 are blind. According to a Gallup survey, blindness is the handicap or disability that Americans fear most following only AIDS, cancer, and Alzheimer's disease.

As the human life span continues to increase and older Americans become one of the fastest growing segments of the U.S. population, deteriorating vision and the associated costs for health and social services have increasingly become an economic burden for families, health service systems, and the Nation in general. A few examples of the extent of vision diseases and disorders follows.

> Collectively, diseases and disorders of the retina are the leading cause of blindness in the United States. Damage to the retina or to its blood supply leads to loss of vision and, when severe, to blindness. Diabetic retinopathy alone is the leading cause of new cases of blindness in adults under age 65, accounts for approximately 12 percent of the new cases of blindness each year in the U.S., and is the major cause of career-disrupting sight loss and blindness among Americans today. About half of the Nation's estimated 14 million people with diabetes have at least early signs of this disease.
>
> Age-related macular degeneration (AMD) is the leading cause of blindness in Americans age 65 and older. Nearly 34 million Americans will be age 65 and older in 1995. Of this total, it is estimated that about 1.7 million will have decreased vision from AMD, and 100,000 will be blind from the disease. Because this age group represents a rapidly growing segment of American society, many eye care professionals expect AMD to become an increasingly important national health problem.
>
> Glaucoma is the second leading cause of blindness in the U.S.; among African Americans it is the leading cause. Approximately two million Americans have glaucoma, and surveys suggest that another one million may not be aware that they have the disease. More than 50 million Americans are at risk for the disease. This potentially blinding condition is associated with increased intraocular pressure and gradual destruction of the optic nerve.

Worldwide, cataract is the leading cause of blindness, disabling 17-20 million people. In the U.S., cataract surgery is the most frequent operation among older persons. Approximately 1.5 million cataract operations are performed annually. More than $5 billion is spent each year for cataract extractions. Unless preventions are discovered, the economic and social burden of cataract will worsen in coming decades as the American population ages.

The diseases and disorders described above are just a cross-section of the extent of the problem and the economic cost. Overall, visual disorders and blindness result in a direct annual cost to the Nation of more than $22 billion.

Accomplishments

Researchers supported by the NEI extramurally and intramurally have made great progress in combatting blinding and disabling eye diseases. Some highlights follow.

Extramural Research

Age-Related Macular Degeneration (AMD). The Macular Photocoagulation Study reported the benefits of laser treatment of blood vessels directly beneath the center of the macula in the "wet" form of AMD. Results considerably extend the treatment eligibility range to include patients who suffer from some of the most severe manifestations of AMD.

Diabetic Retinopathy. Growth factors, which may play a role in the proliferation of abnormal and destructive blood vessels in the retina, have been discovered. A hormone has been identified in the retina which appears to be a potent regulator of retinal blood flow. An initial report of results from a large, population-based epidemiologic study documented the incidence and progression of diabetic retinopathy, and provided important information regarding the eye health care needs of those with diabetes, emphasizing the need for adequate control of hypertension.

Age-Related Eye Disease. To learn more about how AMD and lens opacities develop, researchers have successfully launched the age-related eye disease study (AREDS). The study is well-underway and will include more than 4,600 volunteers.

Cataract. A hypotheses that oxidative stress may play an important role in cataractogenesis has been developed and initially explored. The genes encoding the major proteins of the lens, the crystallins have been characterized, and the chemical changes in these proteins which occur with age elucidated.

Glaucoma. Researchers conducting the Glaucoma Laser Trial reported that laser therapy may be a safe and effective alternative to eyedrops as the first treatment for patients with newly-diagnosed open-angle glaucoma. Long-term follow-up of study patients continues. Because open-angle glaucoma is a chronic disease, study patients will continue to be followed up to three additional years to assess the long-term value of both treatments. If laser treated eyes continue to show effective pressure control, then this treatment would free patients from the daily use of medications, many of which have systemic side effects.

Eye Complications of AIDS. Investigators in a multicenter clinical trial reported that the drugs foscarnet and ganciclovir are equally effective in halting the progression of cytomegalovirus (CMV) retinitis in patients with AIDS. Patients taking foscarnet lived approximately 4.5 months longer, on average, than those taking ganciclovir, suggesting that foscarnet may have some effect in treating the primary HIV infection.

Visual Processing of Motion. Single nerve cells have been found in a specific part of the brain that respond to moving stimuli in the same way that the whole animal does in deciding whether a target is moving or not. The animal's response to targets moving in a given direction can also be influenced by electrical stimulation of that brain area.

Intramural Research

Vision Brain Relationship. NEI scientists have identified a system in the brain that allows the eyes to remain steady when fixating on an object. Understanding this system will provide new clues about how the brain functions to obtain clear vision.

Diabetic Eye Disease. Using nuclear magnetic resonance spectroscopy, NEI scientists have developed a noninvasive technique to measure in the living eye the effect of inhibitors in suppressing the action of aldose reductase, an enzyme implicated in various diabetes complication. This represents an important new tool to evaluate the treatment of diabetic eye disease with these new drugs.

Nephropathic Cystinosis. NEI clinical investigators demonstrated that special eye drops are beneficial in patients with painful and sight-threatening nephropathic cystinosis. This is a disease in which crystals called cystine accumulate in and erode the cornea.

Macular Degeneration. A study of patients with a variety of diseases of the retina has been completed and is yielding important information on the role of environmental and nutritional factors in causing disorders of the eye. Results from the macular degeneration component of the study suggest that patients with higher blood levels of nutrients with antioxidant characteristics such as carotenoids, vitamin C and vitamin E are at decreased risk of the most visually disabling form of macular degeneration. Results from the study also suggest that this leading cause of blindness shares many risk factors with cardiovascular disease.

Opportunities

In vision research, opportunities abound for making advances which will improve the prevention, detection, and treatment of visual disorders, reducing the financial burden, and improving the quality of life for millions of Americans. Since scientific progress produces new opportunities, by its very nature, there will always be more opportunities than can be funded. NEI will therefore continue to invest carefully in those opportunities that show the greatest potential. Some examples follow.

Extramural Research

Age-Related Macular Degeneration. Further basic research to determine the possible genetic, immunological, nutritional, and other factors that make the macula highly susceptible to degenerative diseases. Pursue research on retinal cell transplantation and optic nerve regeneration as potential therapeutic approaches.

Diabetic Retinopathy. Design new aldose reductase inhibitors to prevent the complications of diabetes and to develop molecular genetic approaches to regulate the activity of the aldose reductase gene.

Cataract. Search for ways to augment the lens's natural defense mechanisms which prevent or retard cataractogenesis. Conduct molecular genetic studies to determine how the genetic expression of lens-specific proteins is regulated.

Glaucoma. Exploit advances in molecular biology, cell biology, and immunology to determine the causes of glaucoma and to develop means of prevention. Determine why the rate of glaucoma is higher and the disease is possibly more severe in African Americans. Develop a more effective means for the early detection of glaucoma. Clinical trials are a major tool in this vanguard.

Eye Complications of AIDS. Implement clinical trials of new prophylactic drugs to treat CMV infections, including CMV retinitis; develop oral drugs for treating CMV retinitis.

Assessing Vision in Infants. Evaluate systematically new behavioral, optical, and electrical recording techniques that are making it possible to evaluate visual function in preverbal children and infants who are at risk for developing refractive errors, amblyopia (lazy eye), and strabismus (crossed eyes).

Development of Myopia. Conduct longitudinal studies, including careful evaluation of the optical components of the eye, to identify risk factors for the development of myopia in children and young adults. Laboratory studies of myopia in animal models will reveal the mechanisms of normal and abnormal growth of the eye.

Intramural Research

Retinitis Pigmentosa. Develop gene therapies to treat inherited retinal degenerative disorders, including some forms of retinitis pigmentosa. Develop methods to treat the defective gene in patients with gyrate atrophy, an inherited retinal disease with blinding complications. The success of this project will mark the beginning of a new era in the treatment of genetic ocular diseases.

Eye Complications of AIDS. Further studies of a device that is highly promising for accurately measuring the amount of protein in the anterior chamber of the eye. High levels of protein have been associated in AIDS patients with a blinding viral infection called CMV retinitis. If this procedure proves to be an accurate indicator, clinicians will have a new and easy technique to screen AIDS patients for this disorder, for which drug treatment is available.

Ocular Inflammatory Disease. Conduct a clinical trial to determine whether giving oral doses of S-antigen, a substance in the retina that is thought to initiate inflammatory processes, can build an immunity in patients suffering from ocular inflammatory disease. Such a therapy would allow clinicians to treat sight-threatening inflammations without having to use steroids, which have a number of side effects.

Age-Related Eye Disease Study (AREDS). Assess the incidence, course, and progression of age-related macular degeneration (AMD) and lens opacities in the AREDS study participates. The study includes eleven clinical centers located throughout the country. In addition, a randomized clinical trial will assess the effects of nutritional supplements and minerals on the development of AMD, and the effect of antioxidants on cataract development. The information resulting from AREDS should provide important stepping stones toward preventing these disorders.

These accomplishments and opportunities are just a cross-section of the many achievements, and challenges in vision research. Further details of these and other NEI initiatives are provided under the program activity sections.

Funding for the National Eye Institute during the last five years has been as follows:

	Amount	FTE
FY 1988	$224,947,000	205
FY 1989	234,218,000	210
FY 1990	236,491,000	213
FY 1991	253,445,000	229
FY 1992	270,300,000	247

Purpose and Method of Operation

The National Eye Institute is the single most important source of funds for vision research. Guided by a series of five-year plans, the Institute stimulates and fosters a multidisciplinary basic and clinical, extramural and intramural, vision research and research training program. These initiatives are designed to increase understanding of the normal development, structure, and function of the eye and the visual system and of the causes of eye and visual system disorders and diseases. The goal is to improve the prevention, diagnosis, and treatment of these disorders and diseases, and to enhance rehabilitation, training, and the quality of life of blind and partially-sighted persons.

To help in achieving this goal, basic laboratory and applied clinical research is supported through research project grants, cooperative agreements, research and development contracts, career development awards, institutional training grants, individual training fellowships, and other crosscutting grant mechanisms. The Institute continues its long-standing policy of making individual investigator-initiated research grants its principal support mechanism.

The NEI also conducts an intramural research program at its Bethesda laboratories and clinical facilities. The intramural program resources are unique and frequently focus on eye disorders that are not extensively investigated by extramural scientists. Researchers apply a laboratory and clinical multidisciplinary approach to the study of eye diseases and disorders. This program also includes a biometry and epidemiology component.

To ensure that the public is aware of eye health care advances resulting from the Nation's continued investment and commitment to vision research, the NEI conducts a National Eye Health Education Program.

These combined efforts allow the Institute to effectively and efficiently support a comprehensive, multidisciplinary program of vision research, research training and health education.

Overall Budget Policy

The FY 1993 budget request for the National Eye Institute favors basic research and totals $285,133,000, an increase of $14,833,000 over the comparable FY 1992 estimate. With regard to research project grants, the request will support 1,009 awards. The projected distribution is: 778 noncompeting grants at $148,683,000 and 231 competing grants at $44,135,000. Also, approximately 262 trainees will be funded, the same number that will be supported in FY 1992.

In FY 1993, core grants, physician scientist awards, cooperative clinical research agreements, minority biomedical research support awards, and all other research grants will be supported at the FY 1992 level. Research and development contracts will also be funded at the FY 1992 level.

The request includes $30,705,000 for Intramural Research, and $11,843,000 for Research Management and Support, an increase of $1,485,000 and $553,000 respectively. These funding levels include support for basic operating mandatory requirements including personnel expenses, materials and supplies, animal care facilities, and management fund.

National Eye Institute

Vision Research

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite.

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$217,092,000	$229,790,000	$242,585,000	$12,795,000

Extramural research supported by the Vision Research programs addresses the leading causes of blindness and impaired vision in the United States, including diseases of the retina, corneal diseases, cataract, glaucoma, strabismus, amblyopia, and the special needs of the visually impaired. Funding for Vision Research extramural activities during the last five years has been as follows:

	Amount
FY 1988	$197,308,000
FY 1989	200,474,000
FY 1990	202,431,000
FY 1991	217,092,000
FY 1992	229,790,000

Rationale for the Budget Request

The FY 1993 budget request for the extramural programs in Vision Research is $242,585,000, an increase of $12,795,000 over the FY 1992 estimate. The following are examples of recent research accomplishments made possible by these programs and highlights of some of the many new opportunities which should be pursued.

Retinal Diseases

Overview. The retina, a delicate, light-sensitive tissue at the back of the eye, initiates the process of vision and transmits visual messages to the brain via the optic nerve. Unfortunately, the retina is highly-susceptible to injury in a variety of ways. Damage to the retina or to its blood supply leads to loss of vision and, when severe, to blindness. Diseases and disorders of the retina, collectively, are the leading cause of blindness in the United States. One of these diseases, diabetic retinopathy is the leading cause of new cases of blindness in adults under age 65; another, age-related macular degeneration, is the leading cause of new cases of blindness in people age 65 and older.

Diabetic Retinopathy. In the United States diabetic retinopathy accounts for approximately 12 percent of the new cases of blindness each year.

Diabetes increases the risk of blindness 25-fold over that of the general population, and it is estimated that each year 8,000 Americans become blind as a result of diabetic eye retinopathy.

Wisconsin Epidemiologic Study of Diabetic Retinopathy. A population-based epidemiologic study of the four-year incidence and progression of diabetic retinopathy has been conducted in southern Wisconsin. The study was conducted among insulin-taking persons who were diagnosed with diabetes before age 30. Among the persons initially free of retinopathy, 59% developed the disease by the four-year study visit, and 11% of the 713 individuals initially free of proliferative retinopathy developed this severe disease by the four-year visit. Overall, 41% of the 996 diabetic persons surveyed showed a worsening of retinopathy. Increased blood pressure was shown to almost double the risk for development of retinopathy. Other important risk factors for the onset and progression of diabetic retinopathy were higher levels of an altered form of the oxygen carrying molecule hemoglobin (glycosylated hemoglobin) and longer duration of diabetes. These data provide important information regarding the eye health care needs of those with diabetes and emphasize the need for adequate control of hypertension. The NEI is supporting the continuation of this study to determine the ten-year incidence and progression of diabetic retinopathy, macular edema, and visual impairment.

Cost Savings Estimated. The cost savings to the Federal government (Medicare, Social Security payments, and tax losses) associated with improved detection and treatment of retinopathy and macular edema in patients with Type I (insulin dependent) diabetes has been estimated from epidemiologic and clinical trials data using a computer simulation model. Annual savings of $101 million and 47,000 person-years of sight are predicted based on currently estimated 60% level of screening and treatment; annual savings approximate $167 million and 79,000 person-years-sight if all patients received appropriate care. This estimate of the Federal cost saving is certainly an underestimate of the total cost savings, particularly since so many of the individuals affected are younger than 65 years of age. This research suggests that improvements in eye health education and eye care for people with diabetes would save sight and be cost effective.

Advances in Retinal Cell Biology. Retinal blood vessels contain two types of cells, pericytes and endothelial cells. A decrease in the number of pericytes is a classic early finding in diabetic retinopathy; proliferation of the endothelial cells occurs later in the development of the disease. Some recent experimental studies suggest a possible explanation for these phenomena. First, the growth of pericytes in tissue culture is restricted when glucose levels are elevated. Second, pericytes can inhibit the growth of endothelial cells when the two cell types are in close contact. This growth inhibition appears to be controlled in part by a pericyte-derived molecule called transforming growth factor.

Other growth factors have recently been discovered which may play a role in the proliferation of new, abnormal, and destructive blood vessels in the retina which occurs as a consequence of diabetes. Fibroblast growth factors and insulin-like growth factors have been identified in the retina, and in tissue culture, these factors can stimulate the growth of new blood vessels.

These growth factors have been found to be present in increased amounts in diabetic patients, but additional research is needed to determine if they play a causal role in the development of proliferative diabetic retinopathy.

Aldose reductase. The enzyme aldose reductase (AR) may provide a common link in the pathogenesis of long-term diabetic complications, such as cataract, retinopathy, nephropathy, microvascular disease, and neuropathy. Inhibitors of AR have shown promising results in animal models of diabetes, preventing cataracts, retarding retinopathy, and reversing some aspects of neuropathy. But, the side effects associated with use of the current generation of AR inhibitors limits their clinical application. Therefore, there is a need for improved and innovative approaches to the design of new AR inhibitors. Scientific questions which need to be addressed include determining the three dimensional structure of the AR protein, the structure of its gene, and the details of the regulation of this gene in normal and diabetic tissue.

Age-Related Macular Degeneration. Characterized by the destruction of photoreceptor cells in the macula, a small, specialized area of the central retina, age-related macular degeneration (AMD) is responsible for sharp, crisp vision. A particularly devastating, rapid loss of vision results from a "wet" form of AMD in which abnormal new blood vessels grow beneath the macula, leak, and form scars.

Macular Photocoagulation Study. A series of NEI-supported, randomized, multicenter clinical trials, the Macular Photocoagulation Study (MPS), has previously demonstrated the effectiveness of laser treatment of leaking blood vessels just outside the center of the macular in reducing the rate of visual loss from the "wet" form of AMD. However, clinicians have been uncertain about whether it would be beneficial and safe to treat blood vessels which grow directly beneath the center of the macula. The MPS group has recently reported that laser photocoagulation of these lesions was effective two years after treatment in delaying or preventing deterioration of visual acuity and other measures of visual function. These new results have extended the treatment eligibility range considerably to include patients who suffer from some of the most severe manifestations of AMD.

Age-Related Eye Diseases Study. An NEI-initiated study to learn more about how AMD and cataract develop and progress, the Age Related Eye Diseases Study (AREDS) is well underway. AREDS, which will include more than 4,600 volunteers throughout the Nation, will be the first large-scale attempt to follow the clinical course of these two eye diseases. In addition, the possible role of nutritional supplements and minerals in the development and progression of these two eye diseases will be evaluated in a randomized clinical trial.

Molecular Mechanisms of AMD. Although the cause of this disease is unknown, it is thought to be caused in part by abnormal trafficking of metabolites and cell materials through the retina or a disruption of cell-cell communication which is important for cell function in the macula. Laboratory studies show that lipids accumulate with age in Bruch's membrane, which is located between the retinal pigment epithelial (RPE) and the underlying layer of blood vessels called the choroid, disrupting its structure and altering its fluid permeability. Deposits called lipofuscin accumulate with age in the RPE and it is thought that such accumulation of material may compromise the health of the cell and lead to altered function. It has been shown that under cell culture conditions, the RPE of the macula differs from that of the peripheral retina. The search for RPE-specific proteins using the modern technology of molecular biology is currently an active area of investigation.

Eye Complications of AIDS. Cytomegalovirus (CMV) retinitis is a potentially blinding disease of the retina that affects about 20 percent of people with acquired immunodeficiency syndrome (AIDS). The NEI is currently supporting a randomized, multicenter clinical trial, the Foscarnet-Ganciclovir Cytomegalovirus Retinitis Trial, that was designed to compare the efficacy and safety of two drugs--foscarnet and ganciclovir--used for the initial treatment of CMV retinitis. This comparison was particularly important because ganciclovir cannot be taken with full doses of AZT (zidovudine), the antiretroviral drug most commonly used in the treatment of human immunodeficiency virus (HIV) infection. The trial was designed to evaluate the two drugs for their effects on progression of the CMV retinitis, patient survival, and long-term preservation of visual acuity.

Recently, the study investigators reported that although both drugs appear to be equally effective in halting the progression of CMV retinitis and preserving vision in patients newly diagnosed with the eye disease, the patients treated with foscarnet lived an average of 12.6 months compared to 8.5 months for patients taking ganciclovir. The difference in mortality between the two treatment groups could not be fully explained by the differential use of AZT. These findings suggest that for many patients with AIDS and CMV retinitis, foscarnet may be a better initial treatment than ganciclovir.

The Foscarnet-Ganciclovir Cytomegalovirus Retinitis Trial is being conducted under an organizational umbrella called the Studies of the Ocular Complications of AIDS (SOCA). The goal of SOCA is to expedite the testing of new treatments for CMV retinitis and other ocular complications seen in patients with AIDS. As new antiviral agents become ready for Phase III testing, they can be quickly incorporated into SOCA.

Retinopathy of Prematurity. The leading cause of blindness among premature babies, in the U.S., retinopathy of prematurity (ROP) destroys the sight of 500 of these infants each year. In this disease, blood vessels in the retina increase in number and branch excessively, sometimes leading to hemorrhage and scarring. With improvements in neonatal care over the past two decades, more premature infants, including an increasing number of high-risk, very low-birthweight babies, are surviving and the incidence of ROP has increased.

The NEI-supported Cryotherapy for Retinopathy of Prematurity clinical trial has demonstrated that this treatment halts progression of ROP and reduces by one-half the risk of blindness from the disease. The savings made possible by this clinical trial is estimated to be more than $20 million annually. Long-term follow-up data from the natural history and randomized groups indicate that reattachment of the retina by vitreous surgery, where detachment is due to ROP, had little effect on visual outcome approximately 1 in 3500 live births. The emotional and economic costs of RP to society are enormous; there are no effective treatments for the most common types of RP. Usually RP leads to blindness by age of 60, and sooner in some forms of the disease.

Molecular Genetics of RP. Current technology allows genetic mapping of many inherited diseases to specific chromosomes, offering early diagnosis and counseling opportunities that have not existed previously. One form of X-linked RP was the first of several genes to be mapped by molecular methods. We now know that there are at least two locations for this disease on the short arm of the X chromosome. Separate locations on the long arm of this chromosome are the sites for the genes for choroideremia and color blindness. Chromosome 3 carries the gene for one form of autosomal dominant RP. A remarkable example of research on disease genes has been the discovery of the existence of a gene family responsible for gyrate atrophy. This is one of the few retinal degenerative diseases where the underlying functional defect, a mutation in the enzyme ornithine amino transferase that results in increased synthesis of the amino acid ornithine, was defined well ahead of molecular information on its genomic localization. Molecular analysis now shows that there is one functional gene on chromosome 10 and several related gene sequences on the X chromosome that contribute to this disease. The mechanism by which the genetic mutation in this enzyme causes retinal degeneration is unknown but is an area of active investigation.

Transplantation Research. A significant achievement in retinal degeneration research in animals has been the rescuing of damaged photoreceptor cells by the transplantation of normal supporting retinal pigment epithelium (RPE) cells to the diseased retina. This work has been carried out in a rat mutant in which a defective gene is expressed in the RPE cells. These dramatic experiments are still at a very early stage, but further advances in this area could offer a possible therapeutic approach to some forms of RP and, perhaps, AMD.

Transgenic Approaches. The use of techniques for producing transgenic mice, in which genes from other animals or humans are inserted into the mouse cells and actually expressed in mouse tissue, allow investigators to create experimental models of specific human retinal diseases. This is an important strategy for following up on the identification of defective genes in patients with RP. For example, a mutant rhodopsin gene derived from a patient with an autosomal dominant form of RP was inserted into the genes of mice which now show characteristics of the human disease. The potential of these transgenic mice is enormous in terms of using them to establish the pathogenetic mechanisms involved in the various forms of RP and in developing rational treatment strategies.

Molecular Basis of Signaling in the Retina. Photoreceptor cells of the retina, the rods and cones, are responsible for the capture of light and the initiation of the process of vision. The study of this complex process, which involves a series of chemical reactions called the visual phototransduction cascade, passed a milestone when a precise molecular description of the cascade was defined for the rod cell. Intensive biochemical and physiologic explorations have established the key components of the cascade. Current research has now turned to establishing the complete molecular basis for the termination events of the visual cascade, recovery of sensitivity, and adaptation to constant light levels. NEI-supported scientists have recently discovered a novel protein in the retina, termed recovering, which is sensitive to calcium ions, and which may be a key participant in both the recovery and adaptation processes.

Why are these fundamental studies of photoreceptor cells important? The major diseases of the retina primarily affect the photoreceptors and the underlying retinal pigment epithelium. The highly specialized photoreceptor cells are extremely vulnerable to a variety of insults including, for example, hereditary defects, aging, toxic agents, and dietary deficiencies. As has already been demonstrated in the case of research on retinitis pigmentosa, a clear understanding of the molecular machinery and cellular organization of the photoreceptor cells provides the tools necessary for understanding and combating retinal diseases.

Corneal Diseases

Overview. Diseases and injury to the cornea are the leading cause of visits to clinicians for eye care in the United States and rank among the most painful of eye conditions. Research on corneal diseases includes studies of ocular infections and inflammation, problems with tears and the ocular surface, refractive errors, corneal transplantation, and corneal wound healing.

Ocular Herpetic Infection. Second only to trauma as the leading cause of corneal blindness in the United States today, ocular herpes simplex virus (HSV) keratitis accounts for 500,000 reported cases yearly. The disease affects otherwise healthy, productive individuals, leading to long periods of disability and the need for chronic care associated with approximately $100 million per year in direct medical costs, not counting lost work time.

Following an initial HSV infection, the virus becomes inactive (latent) in nerve cells, only to reactivate unpredictably at some later time causing recurrence of the disease. An important goal of this program is to develop a better understanding of the mechanisms of herpetic latency, leading to new therapeutic approaches. Recent work has led to the discovery of specific herpes virus genes active in the establishment and reactivation of neuronal latency, neurovirulence, and neuroinvasiveness. Understanding the interaction of these viral gene products with neuronal cells may allow researchers to develop strategies for blocking virus reactivation.

Although important work has been done on the development of antiviral therapeutic agents, development of an effective vaccine for the prevention of primary ocular herpes infection is a far more desirable approach. There has been a decided shift in research on ocular HSV infections from studying viral antigens by conventional immunologic techniques to recombinant DNA studies of viral gene expression and structure. As a result of this work, it has been recognized that antibodies to the HSV glycoprotein D appear to protect against primary infection. Further characterization of this vaccine candidate will be important.

Trachoma. The chlamydiae are common infectious organisms of the ocular and genitourinary tracts, and cause a large disease burden worldwide. In the eye, these organisms cause both acute and chronic conjunctivitis, including trachoma, the leading cause of infectious blindness in the world, affecting more than 500,000 people. Recurrent infections elicit pathologic host immune responses, frequently leading to scarring. Enormous cost is associated with chlamydial infections. More than $1.5 billion is expended yearly for these infections in the United States alone.

Although trachoma endemic areas have receded with economic development, the disease is still endemic in Africa and the Middle East and will certainly increase in the next few years as it always has after wars. In the United States, active trachoma exists only in scattered areas of the Southwest. But in rural communities of the developing Nations, where sanitary water and sewerage systems are not always available, this disease imposes severe constraints on economic and social development.

Trachoma is one of the most readily preventable causes of blindness. Yet even though research has identified effective, simple, and inexpensive hygienic control measures, as well as cheap and effective chemotherapeutic agents, the disease continues to spread. Therefore, increasing attention is being devoted to the development of a specific vaccine against C. trachomatis, and a major goal of this program is a detailed understanding of trachoma immunology.

Studies using oral immunization against trachoma have been initiated in several animal species, with considerable recent attention focused on a major outer membrane protein and other glycoproteins as vaccine candidates. A multicenter randomized, double-masked clinical trial has been initiated to compare the effectiveness and side effects of prophylactic agents used in preventing neonatal conjunctivitis.

Dry eye. In most cases, dry eye, a common condition which generally results from insufficient or abnormal tear secretion by the lacrimal gland, causes only mild discomfort. However, in some individuals, the disease may lead to damage and scarring of corneal tissues with ultimate blindness. The public health impact of dry eye is considerable: seven to ten million Americans use artificial tear preparations to counteract this condition.

Dry eye affects both men and women, but is most prevalent in women over the age of 45. Recent studies have led to the hypothesis that reproductive hormones regulate lacrimal gland secretion and that disturbances in this regulation can lead to tear film insufficiency. There is now a major need for research to explore the molecular mechanisms by which specific hormones affect lacrimal gland tear secretion.

Recent results suggest a key role for the peptide hormone prolactin in the development of gender-related differences in lacrimal gland function. Prolactin inhibits normal tear secretion; and estrogens have been shown to enhance, while androgens suppress, prolactin synthesis within the lacrimal gland. Therefore, prolactin inhibition of tear production would be much more pronounced in postmenopausal women, and it would be exacerbated by estrogen therapy without androgens. Ongoing studies are actively exploring the molecular mechanisms by which prolactin affects lacrimal cell fluid secretion.

Cataract

Overview. Worldwide, cataract, a clouding of the age's lens, is the leading cause of blindness, disabling 17-20 million people. In the United States, cataract surgery is the most frequent operation among older people; more than $5 billion is spent each year for lens extractions. The burden of cataract will worsen in coming decades as the American population ages. A major goal of this program, therefore, is to determine how and why cataract develops, search for ways to prevent or slow the progression of cataract, and the development of better treatments and better methods to correct vision after cataract removal.

Oxidative Stress. Recent research has generated findings that have profoundly affected our thinking about age-related cataract. An important hypothesis has been developed that emphasizes the role of oxidative stress in the development of cataract. The function of the various naturally occurring antioxidant systems in the lens has been investigated, but there is a pressing need to explore therapeutic methods for augmenting these defense mechanisms. Epidemiologic studies support this approach, since they suggest that plasma levels of the antioxidant nutrients vitamin E, β-carotene, and vitamin C affect susceptibility to cataract development.

Role of Environmental and Lifestyle Factors. Efforts are underway to identify and quantify environmental and lifestyle factors that are associated with increased risk for the development of age-related cataract. NEI-supported epidemiologic studies of human cataract and studies in animals suggest that such factors as smoking, drugs, sunlight, microwave, X-ray, and ultraviolet radiation exposure may be associated with cataract. Unfortunately, most information on risk factors has come from anecdotal reports or small case-control studies. Therefore, analytic studies are needed to assess the magnitude of these risk factors, and to determine the molecular mechanisms by which they contribute to cataractogenesis.

Molecular Genetics of Lens Crystallins. Loss of transparency in the lens (cataract) has been correlated with changes in the crystallins--three protein families that constitute 90% of the dry weight of the lens. Once produced, the crystallin proteins of the mature lens fiber cell are not renewed. Thus, these proteins must be resistant to the variety of stresses and changes that occur over the individual's lifetime. More detailed knowledge of the structure of crystallins, interactions between them, and how they adapt to environmental and physiological stress is critical to our understanding of how a wide variety of external influences affects the health of the lens. Considerable progress has been made in characterizing the genes that encode the major proteins of the lens, and on describing chemical changes in crystallin protein structure that occur after their initial biosynthesis. Additional studies are needed on the structure and function of the regulatory sequences of crystallin genes.

Glaucoma

Overview. Glaucoma is a potentially blinding condition associated with increased intraocular pressure (IOP) and gradual destruction of the optic nerve. NEI efforts in glaucoma are directed toward preventing blindness

through the development of improved methods for early detection and treatment of the disease, identification of risk factors, and determination of the underlying nature of the disease through basic research.

Glaucoma in Blacks. Recently published results from the NEI-supported Baltimore Eye Study reveal that the prevalence of primary open-angle glaucoma among black Americans is four to five times that of whites. Glaucoma both developed earlier and progressed more rapidly in blacks. These differences were not related to social or economic status or to access to, or use of, eye care services.

Although increased IOP is known to be a risk factor for glaucoma, limited data are available on IOP in black populations. Results from the NEI-supported Barbados Eye Study indicate that there is a higher prevalence of elevated IOP among blacks compared to whites. Increased IOP among blacks was associated with advancing age, systolic blood pressure, a history of diabetes, large body size, and darker complexion.

Glaucoma Laser Trial. The NEI-supported Glaucoma Laser Trial has evaluated the relative efficacy of two treatments for patients newly diagnosed with glaucoma. Patient eyes were randomly assigned to receive either argon laser therapy or eyedrops. If either initial treatment failed to control IOP, additional therapy was prescribed according to a set protocol. Results from two years of patient follow-up suggest that argon laser therapy may be a safe and effective alternative to eyedrops as the first treatment for patients with newly diagnosed glaucoma. However, because open-angle glaucoma is a chronic disease, study patients will continue to be followed up to three additional years to assess further the value of both treatments.

Strabismus, Amblyopia, and Visual Processing

Overview. Developmental disorders such as strabismus (misalignment of the eyes) and amblyopia (commonly known as "lazy eye") affect 2-4% of the U.S. population. In particular, blindness from amblyopia is preventable if the condition is detected and treated early in life. The annual number of surgical operations for strabismus (about 700,000) is exceeded only by cataract surgery. The program supports other important areas of investigation, including neuro-ophthalmological disorders, presbyopia and efforts to prevent and treat refractive errors such as myopia. Understanding visual processing and its disorders requires new knowledge of the visual nervous system, including the molecular, genetic, chemical, cellular, and integrative processes that underlie perception and the control of eye movements.

Epidemiology of Visual Impairment. The NEI-supported Baltimore Eye Study has provided reliable data on the prevalence of blindness and visual impairment in a multiracial population. The results indicate that visual impairment and blindness rise dramatically with age for both blacks and whites, but that the overall age-adjusted rates of blindness and visual impairment among blacks were approximately two times those of whites. There were no differences in rates between men and women. A second project, the Beaver Dam [Wisconsin] Eye Study, confirmed the striking rise in visual impairment with age (0.8 percent in people 43-54, and 21.1 percent in those 75 years or older). In this study, however, age-specific mean visual acuity scores were significantly worse in women than in men. Further investigation is needed to account for the different gender-related findings in the two studies.

Noninvasive Assessment of Visual Function. Technologies for imaging brain activity have provided a valuable new experimental approach. Positron-emission tomography (PET) provides a method for viewing brain activity in awake human subjects. By comparing the activity in various brain regions when a subject views different stimuli, the involvement of particular brain regions in analyzing different types of visual information can be determined. PET has been used to demonstrate the mapping of the visual field onto the primary visual cortex of the brain, and has even led to the exploration of more complex areas of the brain involved in motion processing, the perception of color, and reading. The ability of PET to localize functional specialization in the visual system of living human subjects should greatly extend our understanding of the cortex in health and disease.

Magnetic recordings (magnetoencephalography, or MEG) are another non-invasive approach to localizing human brain activity. The electrical currents generated by neurons create minute magnetic disturbances which can be measured on the scalp with highly-sensitive detectors. These magnetic signals are similar to the electrical signals that can be measured with traditional electroencephalography (EEG), but are far less subject to distortion as they traverse the skull and scalp. Recently-developed MEG systems appear to have good reliability, sensitivity, and temporal resolution. Thus, these systems may prove valuable for defining differential involvement of regions of the human visual cortex in different visual functions.

New approaches to measuring visual fields (perimetry) are also showing great promise. The NEI-supported Optic Neuritis Treatment Trial demonstrated the feasibility of standardizing perimetric techniques, quality control procedures, and data analysis. The ultimate challenge in perimetry is the development of objective measurements of the field of vision that are not dependent on the patient's responses.

Visual Processing of Motion. One of the most active areas of vision research has been directed at understanding how the brain processes moving images. We are constantly moving about in an environment where objects about us are moving in front of our eyes. Finding out how the brain deals with this potentially confusing input has provided us with important fundamental information about how the visual system works, and may have significant implications for understanding neurological disorders of the visual system.

Motion-sensitive nerve cells responding to visual stimuli of particular velocity and direction are located in an area of the visual cortex called the medial temporal area (MT). Minute chemical lesions in area MT of the monkey can both eliminate the animal's perception of motion and degrade smooth, tracking eye movements without affecting other visually-supported functions.

Physiological recordings from these nerve cells during defined visual-behavioral tasks have shown that the threshold for activity from single MT nerve cells is comparable to the behavioral response of the whole animal. The firing rate of an MT cell is correlated with the animal's decision to attend to the visual stimulus. Tiny electrical currents delivered to small groups of MT neurons which are sensitive to a preferred direction of motion can bias the animal's response in a behavioral task involving directional stimuli.

Ocular Motility. Disorders of eye movement are a common symptom of neurological disease and one of the major causes of visual impairment. Understanding oculomotor function is a key step toward treating and ultimately curing strabismus (misalignment of the two eyes) and the many forms of congenital nystagmus (constant oscillating movement of the two eyes). Recent research on monkeys has provided experimental models for the investigation of various kinds of nystagmus and other disorders associated with strabismus. It is now clear that surgically-induced ocular misalignment reproduces both these visual disorders. Early visual deprivation produces a monkey model for congenital nystagmus, latent nystagmus, and strabismus. Studies in patients have revealed new clinical disorders in saccadic eye movements (abrupt voluntary eye movements from one point to another like those used in reading), and have provided data that allow mathematical approaches to understanding disorders of ocular motility. These models have been applied both to diagnosis and evaluation and to the surgical treatment of congenital nystagmus.

Computational Neuroscience. Recent work in computational neuroscience has begun to provide vision researchers with new ways of looking at old questions ranging from how the activity of nerve cells can affect development, to how specific microcircuits in the visual cortex process information. Progress in this field has been enhanced by the fact that computers and computer modeling techniques have become much more powerful and available to more investigators in recent years. The computational approach has been used to model the development of columns of nerve cells in the visual cortex that respond preferentially to input from the left eye or right eye (ocular dominance columns). A similar approach has been used by vision researchers in analyzing the problem of how the visual system perceives curved surfaces when using visual cues from two-dimensional shaded surfaces. Researchers develop their models using data generated from physiological studies of the visual system, an essential approach if the models are to have predictive value.

Assessing Vision in Infants. Behavioral, electro-physiological, and neuroanatomical imaging techniques have been developed to permit evaluation of visual function in preverbal infants and children who were previously untestable. Using these new techniques, investigators have begun to establish developmental norms for a variety of visual functions. While visual acuity has now been well-studied in both normal and clinic populations, work is just beginning on other visual functions such as contrast sensitivity, color vision, and peripheral vision. Investigation of stereoscopic vision is emerging as a particularly useful probe of the developing visual system, since it requires the coordination and functioning of several systems that converge at the cortical level. Rapid techniques for recording visual evoked potentials may prove especially useful for evaluating vision in infants.

One of the greatest challenges in pediatric eye disorders is diagnosing and treating the conditions before they produce irreversible losses in vision. Effective screening procedures that can identify children at greatest risk of developing strabismus or amblyopia, who can then be evaluated more intensively, are currently under development. One of the most promising techniques is a photorefractive procedure that can detect both misalignment of the eyes and refractive errors that may be a risk factor for strabismus and amblyopia.

Origins of Strabismus. Abnormalities in the development of motion processing pathways in the brain have recently been implicated in the subsequent development of strabismus. Older children and adults with this disorder show stronger monocular eye movement and sensory responses to visual targets that move from the side of the head toward the nose (nasally-directed) than in the reverse direction. This directional bias in sensitivity to moving targets is similar to the pattern seen in normal, healthy newborns, who usually then outgrow the asymmetry. Motion pathway testing may prove to be a useful tool for measuring the rate of early binocular development and for identifying infants at risk for strabismus. Motion pathway tests may also prove to be useful as outcome measures when assessing the efficacy of new strabismus treatments.

Development of Myopia. More than 25% of the adult population of the U.S. is nearsighted (myopic). In the worst majority of cases, refractive error develops between ages 6 and 14. A new five-year study of risk factors for the development of myopia has been inaugurated as a cooperative venture between the Orinda Union School District and NEI-supported investigators at the School of Optometry at the University of California at Berkeley. Periodic eye examinations will document the changes over time in the optical components of the eye as well as potential risk factors such as extent of reading or TV watching in all the school children in this Northern California community. Because the residents of this community tend to stay there for many years, it is an ideal setting for a longitudinal study in which the ability to follow the same children for several years is so important. The aim of the study is to develop a way to predict which children are most likely to become near sighted, so that we can devise means to prevent the development of the disorder.

Low Vision. This program also supports research on more effective means to improve the quality of life of visually impaired persons by helping them maximize their use of remaining vision or devising aids to assist those without useful vision. Three million Americans now have chronic visual conditions that are not correctable by eye glasses or contact lenses and that impair everyday function. About 900,000 Americans are legally blind, and approximately 100,000 are totally blind or have only the ability to perceive light but not formed images.

AMD, a leading cause of low vision, poses a particularly difficult problem for vision testing because of the central field scotomas (blind areas) that commonly result from this disorder. Recent developments in the technology for monitoring eye position have made it possible to position a target very precisely on known locations of the retina. This has great potential for both documentation of visual loss and possible retraining of eye movements to enable use of remaining intact parts of the retina.

Progress has also been made in developing new devices for assisting visually impaired persons, e.g., more ergonomically satisfying magnifiers, cosmetically acceptable telescopic spectacles, and voice control and output for computers. Attention now is focussed on devices to assist in the detection of curbs and other obstacles, route-finding, text navigation for both printed materials and computer screens, and computerized image-enhancement.

Underrepresented Minorities in Biomedical Research

The NEI continues to participate actively in trans-NIH Initiatives for Underrepresented Minorities in Biomedical Research by providing administrative supplements to research grants for the support of underrepresented minority scientists and students. The aim of this program is to attract and encourage minority individuals to pursue careers in vision research. Seventeen administrative supplements, totaling more than $582,000 were awarded in FY 1991, an increase of 26.5% over the FY 1990 level of support; the level is expected to increase again in FY 1992 and FY 1993, a total of about $611,000 and $654,000 respectively. The NEI Extramural and Collaborative Program staff participate regularly in conferences and national meetings that provide special opportunities to counsel minority students and investigators about possible research training and career development opportunities in vision research. The NEI, in cooperation with the Association for Research in Vision and Ophthalmology, has initiated a new competitive program which provides travel support for underrepresented minority graduate students and postdoctoral fellows to attend national scientific meetings. The NEI co-funds grants in the National Institute of General Medical Sciences' Minority Biomedical Research Support Program, and in FY 1992 will co-sponsor a Request for Applications for NRSA Individual Predoctoral Fellowships for Minority Students.

National Eye Institute

Intramural Research

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite.

Budget Authority:

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
164	$26,532,000	174	$29,220,000	180	$30,705,000	+6	+$1,485,000

The Intramural Laboratory and Clinical Research program of the National Eye Institute consists of eight components: the Clinical Branch, the Ophthalmic Genetics and Clinical Services Branch, the Laboratory of Immunology, the Laboratory of Mechanisms of Ocular Diseases, the Laboratory of Molecular and Developmental Biology, the Laboratory of Retinal Cell and Molecular Biology, the Laboratory of Sensorimotor Research, and the Laboratory of Ocular Therapeutics. This budget activity also includes the Biometry and Epidemiology Program.

The NEI intramural program has developed a broad multidisciplinary research effort on blinding and disabling disorders of vision that integrates laboratory and clinical research in such areas as ocular inflammatory diseases, diabetic retinopathy, developmental and degenerative disorders of vision, cataract, and the effects of neurological defects on vision.

Funding for intramural research during the past five years has been as follows:

	Amount	FTE
FY 1988	$19,723,000	141
FY 1989	22,375,000	144
FY 1990	24,345,000	150
FY 1991	26,532,000	164
FY 1992	29,220,000	174

Rationale for the Budget Request

The FY 1993 budget request for intramural research is $30,705,000, an increase of $1,485,000 over the FY 1992 estimate. This level will provide funds for pay related increases and for inflationary costs associated with the purchase of research supplies and services.

Vision Brain Relationship

Research in the Laboratory of Sensorimotor Research focuses on the systems within the brain that integrate visual information for perception and for the generation of eye movements. Scientists in this laboratory have recently identified and defined what they believe is a previously unrecognized oculomotor system that keeps our eyes steady during periods when we fixate on an object. Investigators have been able to define the role of this fixation-related zone by recording the activity of single cells in the region of the brainstem in awake monkeys while activating and deactivating the cells by controlled stimulation. Since virtually all visual information is obtained during periods of visual fixation, these studies provide clues about how the brain functions to obtain clear vision and may lead to important findings that can help overcome defects affecting this system.

Diabetes Ocular Complications

Scientists in the Laboratory of Ocular Therapeutics have been studying methods to suppress the action of aldose reductase, an enzyme that has been implicated in diabetic complications, including diabetic retinopathy. Toward this goal, they are working to develop new classes of drugs to control aldose reductase activity without the side effects that current inhibitors cause. As part of this research, they also have collaborated with scientists in the National Heart, Lung and Blood Institute to develop a noninvasive procedure for assessing aldose reductase activity in the lens, using nuclear magnetic resonance spectroscopy. They have used this procedure successfully to measure aldose reductase in the lenses of normal animals as well as those that have diabetic-like conditions. This technique has potential for clinical application because it allows scientists to monitor quantitatively the amount of aldose reductase is the intact, functioning lens. In addition, it can be used to assess the effect of aldose reductase inhibitors in controlling aldose reductase in the lens and may also provide a means for assessing the action of anti-cataract drugs.

Ocular Genetic Diseases

The Ophthalmic Genetics and Clinical Services Branch conducts a multi-faceted clinical research program focusing on genetic diseases of the eye and visual system and cataracts, with a commitment to translating the results of laboratory research to the improvement of patient care. In recent studies, investigators have discovered that ocular cysteamine drops have a beneficial effect in patients with painful and sight-threatening nephropathic cystinosis. Promising data have also been collected to support the hypothesis that diets low in the amino acid arginine may be effective in slowing the development of blinding chorioretinal atrophy. This has been particularly striking in the detailed evaluations of younger siblings who have been on these diets over half their lives and who have much less ocular involvement than did their older siblings at comparable ages. This work illustrates the successful transfer of knowledge obtained through basic research to provide treatment for a hereditary disease affecting sight.

Genetic Therapies

Collaborative studies between the Ophthalmic Genetics and Clinical Services Branch and the Laboratory of Immunology are now underway to develop a treatment to correct the ocular defect in gyrate atrophy, an inherited disease in which excessive amounts of the enzyme ornithine are produced and cause complications that include blinding retinal degeneration. Investigators are now working simultaneously on developing an animal model of gyrate atrophy and developing methods to correct the defective gene. Their work is progressing rapidly, and investigators project that they may have a clinically acceptable treatment available for human testing within the next two years. The success of this project would mark the beginning of a new era in the treatment of inherited ocular diseases.

AIDS

The Laboratory of Immunology is conducting a number of clinical investigations in the treatment of cytomegalovirus (CMV) retinitis, an ocular complication affecting 20-30 percent of all AIDS patients. Since CMV is presumed to be a blood-borne virus, higher amounts of protein would be found in the eyes of CMV retinitis patients due to breaks in the blood retinal barrier. Investigators are experimenting with the use of the Kowa cell/flare meter to measure the amount of protein in the anterior chamber of the eye in patients with and without CMV retinitis. Those with CMV retinitis appear to have higher amounts of protein in the anterior chamber, and a screening of AIDS patients with this instrument is now being conducted to see if these elevations in protein will be a sensitive indicator of early CMV retinitis. If this is verified, this procedure can be used as an easy screening device that may resolve the problem of how often one needs to examine AIDS patients for the potentially sight-threatening disorder.

NEI clinicians have been examining the possible ocular effects of ddI, another antiretroviral drug that has been conditionally approved recently by the FDA for treating HIV infection. They examined both pediatric and adult patients who have been treated with ddI, and determined that some of the children developed a progressive retinal atrophy that was reversible after ddI was discontinued. To date, such toxicity has not been found in adults taking ddI.

Clinicians in the LI have demonstrated that ganciclovir is effective in treating CMV retinitis. However, systemic treatment with ganciclovir cannot be used in patients who take AZT, the primary drug used in treating AIDS, because both drugs depress bone marrow function. Further, the vaso-occlusive nature of the retinitis itself results in occlusion of the vessels (retinal arterioles) that are at least partially responsible for the delivery of systemically administered drugs to the eye. This may result in lower levels of drug reaching the infected retina, particularly in the late stages of the disease. Injection of ganciclovir directly into the eye has been effective in halting the progression of the disease. The short half-life of the drug, however, necessitates one to two intraocular injections a week to maintain therapeutic levels. Widespread use of this technique has been limited by the logistical difficulties and inherent risks associated with numerous intraocular injections.

A new device has been developed that can be implanted into the eye via a relatively minor surgical procedure. Once implanted, this device will release ganciclovir directly to affected ocular tissue for a period of up to four months. Preliminary experience indicates that this method of drug delivery should avoid the problems of systemic toxicity. Investigators in the LI plan to conduct a trial of this device to determine its efficacy in treating CMV retinitis.

Ocular Inflammatory Diseases

Another major focus within the Laboratory of Immunology is the treatment of a group of ocular inflammatory diseases, known collectively as uveitis, that are responsible for approximately 10 percent of all legal blindness in the U.S. Using an animal model of experimental autoimmune uveitis that was developed by scientists in this Laboratory, investigators successfully reversed the inflammation by "vaccinating" the animals with oral doses of S-antigen, the substance in the retina that is thought to initiate the inflammatory process. This work proved that ocular inflammatory diseases can be manipulated effectively in animals by the oral administration of S-antigen, a human clinical trial of this methodology is anticipated.

Cataract

The Laboratory of Mechanisms of Ocular Diseases concentrates on biochemical and molecular studies of cataract. Recently, scientists uncovered a mutant form of protein in the lens of a strain of guinea pig that spontaneously develops cataract. Studies are now being conducted to determine what causes the mutation and how it may cause the opacification of the lens. Molecular studies are also being conducted in a mouse model of cataract and findings to date offer great promise in understanding the cataractogenic defect. Other scientists in this Laboratory are conducting molecular studies to characterize aldose reductase (AR), the enzyme implicated in such diabetic complications as cataract, retinopathy, and neuropathy. Although several AR inhibitors have been developed, their side effects and lack of efficacy in clinical trials have emphasized the need for continued and innovative approaches to AR inhibition. Investigators have focused on elucidating the structural aspects of AR and its mode of expression; with such information, they hope to be able to develop new genetic therapies that will inhibit or prevent the debilitating complication of diabetes.

Investigators in the Laboratory of Molecular and Developmental Biology have solved the structure of the gene that encodes the main intrinsic human lens membrane protein and have begun studies of the mechanism of its expression. These studies are directly relevant to our understanding of gene expression, aging, and cataract development in the human lens.

Visual Pigment Regeneration

Recent studies conducted in the Laboratory of Retinal Cell and Molecular Biology have given definitive physiological proof that a protein called Interphotoreceptor Retinal-Binding Protein (IRBP) actively participates in the visual process. In a recently published study, investigators demonstrated that IRBP is a "shuttle" for retinoid. IRBP-mediated transfer of retinoid was shown to control the recovery of sensitivity of the photoreceptor after light bleaching in intact, functioning photoreceptor cells. In addition, with concentrations of IRBP and retinoid in the physiological range, electrophysiological recovery occurs in a manner and within the timeframe seen in the intact eye. This work uncovered new and important differences between rod and cone neuronal functioning by elucidating separate pathways for visual pigment regeneration in the two types of photoreceptors.

Biometry and Epidemiology Program

The primary mission of the Biometry and Epidemiology Program (BEP) is to plan, develop, and carry out human population studies concerned with the cause prevention, and treatment of eye diseases and vision disorders. This includes studies of incidence and prevalence in defined populations, prospective and retrospective studies of risk factors, natural history studies, clinical trials, genetic studies, and studies to evaluate diagnostic procedures. The SEP also carries out a program of education in biometric and epidemiologic principles and methods for the vision research community, and provides biometric and epidemiologic assistance to the NEI scientific staff.

The Biometry and Epidemiology Program is initiating a prospective cohort study, called the Age-Related Eye Disease Study (AREDS), designed to provide information on the development (incidence), course, and progression of age-related macular abnormalities and lens opacities. The study will also evaluate various possible risk factors for the development and/or progression of the two disorders. In addition, a multicenter, randomized clinical trial will assess the effects of nutritional supplements and/or minerals on the development and progression of age-related macular degeneration (AMD) and on cataract. Eleven clinical centers, enrolling 4,600 eligible participants to be followed for at least seven years, will participate in this phase of AREDS. The information resulting from AREDS should provide important stepping stones toward preventing AMD and cataract.

A study of patients with a variety of diseases of the retina has been completed and is yielding important information on the role of environmental and nutritional factors in causing disorders of the eye. Results from the first component of the study suggest that patients with higher blood levels of nutrients with antioxidant characteristics such as carotenoids, vitamin C, and E vitamin are at decreased risk of the most visually disabling form of macular degeneration. Results from the study also suggest that this leading cause of blindness shares many risk factors with cardiovascular disease. The study is also identifying risk factors for other retinal disorders that result in severe vision loss--branch retinal vein occlusion, central retinal vein occlusion, retinal detachment, and macular holes.

The NEI joined with the U.S. National Cancer Institute and the Cancer Institute of the Chinese Academy of Medical Sciences, to conduct eye examinations in central China at the end of a five-year randomized trial of vitamin/mineral dietary supplements. Almost 6,000 adults were examined to see if that nutritional intervention might reduce the occurrence of age-related cataract and age-related macular degeneration. Data analysis is in progress.

National Eye Institute

Research Management and Support

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite.

Budget Authority:

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
65	$9,821,000	73	$11,290,000	75	$11,843,000	+2	+$553,000

The Research Management and Support (RMS) budget activity provides resources for the immediate Office of the Institute Director, the Extramural and Collaborative Program (ECP), and certain functions of the Office of Administrative Management. The concerted efforts of these components ensure the effective and efficient management of NEI programs, allowing the Institute to identify and address more effectively opportunities and needs in vision research, and to maintain and improve upon the productive working relationships that have been established with the research community and other interested individuals and organizations.

This activity encompasses a wide range of responsibilities. Included among them are managerial functions: planning, directing, coordinating, and evaluating Institute-wide programs and policies; review and administration of research and training grants, contracts, and cooperative agreements; and coordinating collaborative research activities involving NEI staff and extramural investigators. Centralized financial management and personnel management, the Office of Science Policy and Legislation, the Office of International Program Activities and the National Eye Health Education Program are also funded through this activity. In addition, this budget activity includes support for the National Advisory Eye Council.

Funding for Research Management and Support during the last five years has been as follows:

	Amount	FTE
FY 1988	$ 7,804,000	64
FY 1989	8,408,000	66
FY 1990	9,681,000	63
FY 1991	9,821,000	65
FY 1992	11,290,000	73

Rationale for the Budget Request

The FY 1993 budget request for Research Management and Support is $11,843,000, an increase of $553,000 over the 1992 estimate. This request includes the cost of services provided centrally, personnel expenses, materials, supplies, and other basic operating needs.

Vision Research--A National Plan

During this fiscal year work continued on the further development and final preparation for publication of the National Advisory Eye Council's Vision Research--A National Plan: 1992-1996. The Plan will include an extensive and comprehensive survey of current needs and opportunities in the many and diverse sciences that vision research comprises, with the overall goal of advancing knowledge that will improve the prevention, diagnosis, and treatment of blinding and disabling eye diseases and disorders. For each of NEI's major disease-oriented research programs and subprograms--as well as for the special area of Low Vision and Its Rehabilitation--the Plan states goals and objectives, documents recent accomplishments, and, most significantly, lists those specific key questions whose answer, according to a consensus of experts, will advance us much further along the path toward solving the great remaining problems of blindness, visual impairment, and visual disability in the United States.

The Plan will also include discussion of important policy issues facing the NIH especially as they apply to the National Eye Institute, including scientific training and research manpower development, scientific integrity, participation of minorities in vision research, and research involving animals. Also, because during this period work was underway throughout NIH on developing the new NIH Strategic Plan, the NAEC's plan for the NEI will be modified to address specifically the Promising Areas of Science that were identified through the NIH strategic planning process to which the NEI was a major contributor. In so doing the NAEC's Plan, though focused on and emphasizing NEI's mission and program concerns, will be aligned and consistent with the priorities of corporate NIH.

International Activities

The specific objective of NEI's international program is to facilitate the development and worldwide application of appropriate NEI-supported research. NEI currently supports research internationally on four blinding diseases with major worldwide impact: cataract, onchocerciasis, glaucoma, and prolonged vitamin A deficiency leading to keratomalacia or xerophthalmia.

Data from NEI-sponsored case-control studies of aging-related cataract in the U.S., Italy, and India, which explored the possibility of personal and/or environmental risk factors, were recently analyzed. Inter-country comparisons continue in an effort to determine why the onset of cataract occurs at earlier ages in some geographic areas. Follow-up and natural history studies are in progress in Italy and the U.S. with the hope of designing interventions to delay the progression of cataract.

For many years, NEI has worked with non-governmental organizations on eye health and prevention programs in Latin America and the Caribbean. The Institute continues to provide consultation to Cataract Free Zone projects in nine Latin America countries. NEI is now supporting the Barbados Eye Study, a population-based epidemiologic study aimed at preventing or delaying the onset of glaucoma and other eye diseases, and to learn why Blarks are at particularly high risk from glaucoma. This investigation, conducted with the Barbados Ministry of Health, is the first comprehensive evaluation of glaucoma and other eye diseases in Barbados.

NEI supports intramural and extramural investigators who are attempting to determine those antigens in the adult and larval forms of the worm that are responsible for the host immune response and for the ocular and systemic complications of onchocerciasis, the third major cause of preventable blindness in the developing world. Intramural scientists are performing immunological and histopathological studies on ocular biopsy material from patients with onchocerciasis and from controls living in the same location.

Clarifying the role of vitamin A deficiency in child health and survival and defining successful, sustainable control measures have broad worldwide public health importance. NEI has provided technical assistance to a randomized, controlled, masked clinical trial in southern India involving 15,419 preschool-aged children. The risk of death in the group treated with a supplement of vitamin A, at a level potentially obtainable in food, was less than half that in the control group.

National Eye Health Education Program

This year, the National Eye Health Education Program (NEHEP), coordinated by the National Eye Institute, had continued success in the development and implementation of program activities for individuals and groups at high risk for glaucoma and diabetic eye disease. The initial target audiences for glaucoma education are Blacks over age 40 and anyone over age 60; and for diabetic eye disease programs, all people with diabetes. The NEHEP is conducted in partnership with 37 public and private organizations.

NEHEP accomplishments this year have included completion of a national survey of the public's knowledge, attitudes and practices about eye health and disease; development of information and education strategies and materials for the glaucoma and diabetic eye disease programs; and development of an applied research program for diabetic eye disease education.

The Second National Eye Health Education Conference was convened in February 1991. Participants were presented an overview of the latest scientific information and the elements of the proposed education and information activities. The Conference provided participants the opportunity to review materials and to make recommendations for the further development of the glaucoma and diabetic eye disease programs. In addition, participants described how their organizations will become involved in the implementation the NEHEP. Plans are now being developed for a third national conference to be convened in Fall of 1992. This conference will give participants the opportunity to share experiences in the implementation and evaluation of eye health education projects including those designed to reach special populations. The NEHEP Partnership has been involved throughout the development of the program, and will participate in the program implementation, including dissemination of materials, co-sponsorship activities, and participation in applied research projects.

Following the conference, NEHEP staff developed strategies and materials designed to reach the NEHEP target audiences through community, mass media, and interpersonal channels. These include education kits; program guides, brochures and posters; public service announcements (PSAs) for television, radio, and print media; and a continuing education program for pharmacists. In November 1991, the pharmacy continuing education program on diabetic eye disease was published in a professional journal that reached 100,000 pharmacists. The public service campaign was released in January 1992.

The NEHEP was formally launched by Secretary of Health and Human Services Louis W. Sullivan at a national press conference in December 1991. At that time, eye examination recommendations for individuals at risk for glaucoma and diabetic eye disease were released as well as results from the national survey for people at risk for glaucoma. Extensive media coverage resulted from the press conference and NEHEP staff are counting on their efforts to publicize this national program.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Detail of Permanent Positions

	1991 Actual	1992 Estimate	1993 Estimate
ES-5.............	1	1	1
ES-4.............	5	5	5
ES-3.............	0		
ES-2.............	1	1	1
ES-1.............	0		
Subtotal	7	7	7
GS/GM-15.........	20	20	20
GS/GM-14.........	21	22	23
GS/GM-13.........	16	19	22
GS-12............	16	18	19
GS-11............	16	21	21
GS-10............	0	1	1
GS-9.............	18	21	21
GS-8.............	7	7	7
GS-7.............	19	21	21
GS-6.............	6	8	8
GS-5.............	2	5	5
GS-4.............	2	2	2
GS-3.............	1	1	1
GS-2.............	1	1	1
Subtotal........	145	167	172
Grades established by Act of July 1, 1944 (U.S.C. 207):			
Assistant Surgeon General.......			
Director Grade....	2	3	3
Senior Grade......	1		
Full Grade........			
Senior Assistant Grade............	2	2	2
Assistant Grade...			
Subtotal.........	5	5	5
Ungraded.........	1	1	1
Total permanent positions.......	158	180	185

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

New Positions

	1993		
	Pay Plan/ Grade	No.	Salary
Intramural Research			
Staff Fellows:			
Geneticist	AD	1	$30,000
Molecular Biologist	AD	1	30,000
Ophthalmologist	AD	1	30,000
Chemist	AD	1	30,000
		4	120,000
Research Management and Support			
Health Economist/Program Analyst	GS-7	1	22,717

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Increases in Positions

Additional positions are requested to explore opportunities in high priority areas like gene therapy, diabetic retinopathy, age-related eye diseases including cataract, immunology, and National Eye Health Education Program activities. Areas that have the potential for big payoffs in terms of reducing human suffering, health care and related costs, and major opportunities for improving the quality of life and prolonging earning power of our aged citizenry. These opportunities have taken years to generate, and offer tremendous return on the Nation's steadfast investment in vision research.

NEI would hire geneticists, ophthalmologists, chemists, and molecular biologists. These positions are necessary for the gene therapy and age-related eye diseases initiatives. As the mapping and sequencing of the human genome progress, the number of diseases which may be able to be treated are expected to increase substantially. Gene therapy offers hope for effective treatment against such diseases. Opportunities are at hand in age-related eye diseases and disorders, such as cataract, diabetic retinopathy, glaucoma, and age-related macular degeneration.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Amounts Budgeted for Increases in Full-Time Equivalents

ACTIVITY/POSITIONS	Pay Plan/ Grade	No. of Pos.	O.C. 11 Annual Salary	O.C. 12 Benefits	O.C. 21 Travel	O.C. 23.1 O.C. 23.2 Rent	O.C. 23.3 Comm./ Util.	O.C. 25 Other Services	O.C. 31 Equip.	Other Objs.	Subtotal New Costs	Support Staff Share	Number of FTEs	TOTAL NEW COSTS
Intramural Research														
Staff Fellows:														
Geneticist	AD	1	$30,000	$4,800	$0	$0	$0	$0	$0	$0	$34,800	$0	2.00	$69,600
Molecular Biologist	AD	1	30,000	4,800	0	0	0	0	0	0	34,800	0	2.00	69,600
Opthalmologist	AD	1	30,000	4,800	0	0	0	0	0	0	34,800	0	1.00	34,800
Chemist	AD	1	30,000	4,800	0	0	0	0	0	0	34,800	0	1.00	34,800
		4	120,000	19,200	0	0	0	0	0	0	139,200	0	6.00	208,800
Research Management and Support														
Health Econ./Prog. Analyst	GS-7	1	$22,717	$5,225	$0	$0	$0	$0	$0	$0	27,941	0	2.00	$55,883
		1	22,717	5,225	0	0	0	0	0	0	27,941	0	2.00	55,883

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Advisory and Assistance Services

The Advisory and Assistance Services activity provides ongoing support for standing and ad hoc committees that review and evaluate research project grants, contracts and intramural projects for technical merit. Under the studies, analyses, and other evaluative activities category, operations research services are supported. Experts and consultants are used to advise the Institute in the conduct of data monitoring committees, on clinical trials, and other similar ad hoc advisory activities. The Institute will continue to support individual experts and consultants, studies, analyses, and other evaluative activities. Among these initiatives is support for technical evaluation panels. The process of technical evaluation is a requirement of the NIH Peer Review process in assessment of various proposals, both in station support and research contracts. The personnel appointments category includes support for meetings of the National Advisory Eye Council (NAEC).

Tuesday, March 24, 1992.

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

WITNESSES

DR. LAWRENCE E. SHULMAN, DIRECTOR, NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

DR. JAY MOSKOWITZ, ASSOCIATE DIRECTOR, SCIENCE POLICY AND LEGISLATION

DR. STEVEN J. HAUSMAN, DEPUTY DIRECTOR, NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

MARGARET S. KERZA-KWIATECKI, ACTING EXECUTIVE OFFICER AND BUDGET OFFICER, NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

DENNIS P. WILLIAMS, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTRODUCTION OF WITNESSES

Mr. Natcher. At this time we take up the budget request for the fiscal year 1993 for the National Institute of Arthritis, and we have before the Committee Dr. Lawrence E. Shulman, the Director. Dr. Shulman, you have appeared before our Committee on many occasions. We are glad to have you.

Before you give us your statement, Dr. Shulman, tell us who you have with you there at the table.

Dr. Shulman. Yes, Mr. Chairman.

To my left is Dr. Steven Hausman, Deputy Director of our Institute; Ms. Margaret S. Kerza-Kwiatecki, who is the Acting Executive Officer and Budget Officer of our Institute; and Dr. Jay Moskowitz, who is the Associate Director of the NIH for Science Policy and Legislation; and Mr. Dennis Williams, who is, as you know, Deputy Assistant Secretary for the Budget, Department of Health and Human Services.

Mr. Natcher. Thank you, Dr. Shulman.

Now, Doctor, we will be pleased to hear from you.

Opening Statement

Dr. Shulman. Good morning, Mr. Chairman.

It is a great pleasure and privilege to appear before you today to report to you on the activities of NIAMS and to share with you some of our future plans.

As reflected in the name of the Institute, our research programs are rich and diverse. They address the very components of the body—the joints, muscles, bones, connective tissues, and the skin—that are fundamental to human structure, form, and movement.

Our programs provide a research agenda and focus for over 100 rheumatic diseases, the many diseases of the musculoskeletal system, and the numerous diseases of the skin.

The research mission of this Institute encompasses a wide number of the most painful, disabling, distressing, and disfiguring diseases and disorders that touch Americans. We are pleased to report to you some of our recent research advances and accomplishments, and our current challenges and opportunities.

This has been a busy year, Mr. Chairman. Much has been happening. We have had many new findings. We have been hard at work planning for the future.

You have our written statement, sir, for the record. May we place this in the record, please?

Mr. NATCHER. In its entirety.

Dr. SHULMAN. Thank you.

We have outlined progress in many areas. I have selected four areas to discuss with you today.

Let us start with new developments in osteoporosis as you see on Poster 1. Osteoporosis is the leading cause of bone fractures in women and the elderly.

[The information follows:]

Osteoporosis

New Developments

- Women's Health Initiative
- Estrogen receptor on bone cells: discovered
- Bisphosphates, promising
  - prevention
  - treatment
- Calcitriol (Vitamin D metabolite) effective
- Calcitonin: bone receptor gene discovered
- Exercise plus calcium: some benefit
  - build up bone mass
  - retard bone loss

POSTER 1

Nothing is more important to this Institute, sir, than this eminently preventable disease, which has such a big societal impact. We are committed in this Institute to cutting the number of fractures to the bone.

We are a major player in the NIH Women's Health Initiative, so admirably launched by Dr. Healy. Dr. Joan McGowan, Director of the Bone Diseases and Bone Biology Branch, who is here, spends a large portion of her time and efforts on this major initiative.

The questions of benefits versus risks of hormone replacement therapy in women are being addressed by this appropriately ambitious program. In recent years, we have proven that estrogen replacement in women prevents both bone loss and bone fractures, but until now we did not know how.

This year we have found receptors for estrogen on those bone cells, the osteoclasts, that eat away the bone. This is hopeful. If we can find out how this works in detail, then we can find a new way to achieve prevention of bone loss with agents other than estrogen for those women, such as those who have a risk of breast cancer, for whom it is inadvisable to take estrogen.

Bisphosphonates can retard bone loss. Drug firms are developing second and third generation bisphosphonates that may not only prevent bone loss, but also may be able to restore lost bone. There is a new report this year that calcitriol, a derivative of vitamin D, may prevent bone loss.

We have a new lead concerning calcitonin, which is a hormone widely used in Europe for bone loss. Scientists in Boston have found the gene for the receptor for calcitonin on bone cells.

We also have encouraging results on exercise and calcium. In research on twins, giving twice the normal amount of calcium builds greater bone mass than in those who just take the recommended amount. There is a New England Journal of Medicine report showing that the combination of exercise and extra calcium blunts bone loss in middle-aged women. There is progress in this area.

Now, for progress in rheumatoid arthritis, which as you know is the major crippler causing inflamed, swollen and tender joints. Let's first review how much our scientists have accomplished in recent years with your support, as shown on Poster 2. We are responding more fully to the question posed by you last year on this very question.

[The information follows:]

Rheumatoid Arthritis

Achievements

- New and broader range of drugs
  - NSAIDs, methotrexate
- Effective joint replacements
  - knee, hip, fingers
- Sharp reduction in incapacitation
- Understanding joint inflammation
- Understanding joint destruction
- Understanding genetic susceptibility
- Potential infectious triggers
- Recognizing role of nervous system

POSTER 2

First, what are our achievements? We have more and better drugs, new non-steroidal antiinflammatory drugs for mild to moderate arthritis. For those with more severe arthritis, we have second-line drugs such as methotrexate, which are very effective.

Joint replacements are a great success. Not only do they relieve pain but they restore people to active useful lives. We put in new hip, finger, and knee replacements. We know how much help Mr. Conte received from his replaced knee. He told us about that.

As a result, we don't see as many people who are severely disabled with rheumatoid arthritis as we used to see. Far fewer are bedridden or confined to the wheelchair.

We have a better understanding of how joints become inflamed and the mechanisms by which they are destroyed.

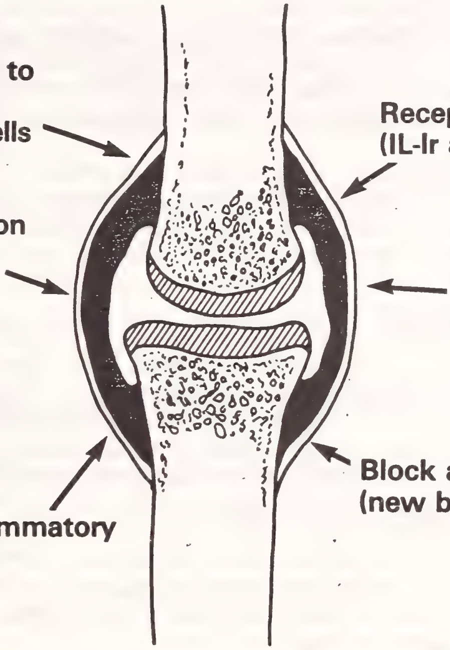
We have uncovered underlying genetic factors and identified a few potential infections as triggers. We have recently recognized the possible role of the nervous system. I can go into that further a little later, if you wish.

As a result, we have several new strategies for attacking rheumatoid arthritis. These strategies are undergoing intense active investigation. I have listed them here on this diagram of a joint on Poster 3.

[The information follows:]

Rheumatoid Arthritis

New Ways to Attack It



Antibodies to destructive immune cells (Anti-CD4)

Receptor blockers (IL-Ir antagonist)

Block production of interleukin-1 (TENIDAP)

Inhibitors of destructive enzymes

Block angiogenesis (new blood vessels)

Novel anti-inflammatory agent (NOVA)

POSTER 3

This is a diagram of a joint, such as the knee, in which two bones are opposing one another.

Cartilage is on the end, as you can see. They are surrounded by the joint lining, which is shown in red. That joint lining is thickened with inflammation as shown in red.

This is what causes patients to have hot, swollen, tender and painful joints. Now, the inflamed lining is packed with white blood cells called lymphocytes. Many have a protein called CD–4 on their surface. When a large number of antibodies to CD–4 are produced by monoclonal techniques and injected intravenously, there is a sharp drop in the number of these cells and then a decrease in arthritis.

This was first shown in mice and now reported for the first time last fall in patients with rheumatoid arthritis.

There is also a substance called interleukin-1, that directs cells to produce enzymes that destroy the cartilage and the bone. There is a new drug that has been developed to block the production of interleukin-1 in the joint.

Another approach is to block the receptor for interleukin-1 on the cells. Such an antagonist has been developed in Colorado, and it is being investigated at the present time.

Another approach is to knock out the destructive enzymes that destroy the cartilage, such as the enzyme collagenase. We are now supporting a clinical trial using this treatment for rheumatoid arthritis in six centers. There are two other major strategies, which I could address later if you wish.

Now let's turn to lupus, a serious disease affecting mostly young women. This is a major autoimmune disease in which the immune system mistakenly attacks the body's own tissues. We have made significant progress as seen on Poster 4.

[The information follows:]

Lupus (SLE)

Achievements

- Great increase in survival
    - early diagnosis
    - better treatment
- Improved quality of life
    - pregnancy
- Immune abnormalities discovered
- Special forms uncovered
- Life-saving treatments
    - i.v. cyclophosphamide

POSTER 4

Lupus used to be a highly fatal disease. Now over 90 percent of women survive 10 years after diagnosis, due to better diagnosis, tests, and treatments. The quality of life has vastly improved. Many can lead active lives and some can have successful pregnancies.

We have found that lupus is not just one disease because we found special forms that occur in infants or a special form that affects the skin, for the most part.

Our intramural scientists have found life-saving treatments. Yet there are many unresolved questions on its cause, factors of gender and race, and some patients still die.

Therefore, we have developed special initiatives this year to combat lupus as shown on Poster 5.

[The information follows:]

Lupus (SLE)

Current Initiatives

- Scientific Workshop: Future Research Agenda
- Lupus team convened
- Anti-phospholipid Antibody Workshop
- SLE in special populations
- "What Black Women Should Know About Lupus"
    - — public education (targeted)
    - — professional education (targeted)

POSTER 5

This was stimulated by the keen interest of this Committee, in particular, Mr. Pursell and Mr. Stokes, for which we are grateful.

This past January, I convened 50 top experts on lupus in a scientific workshop to generate a new research agenda. New opportunities and scientific directions were developed at the workshop. These were reviewed by an external advisory group and by a lupus research team that I formed.

We also held a special workshop on antiphospholipid antibodies that are important to pregnancy and clotting problems.

We are generating epidemiologic studies in special populations, especially black and Hispanic women. We continue to expand the educational activities of our Lupus Task Force in Minority Populations. The booklet you have at your desk there, Mr. Stokes, 30,000 of those have already been distributed.

I would like to outline briefly for you on Poster 6 the recommended further research directions.

[The information follows:]

Lupus (SLE)

Research Directions

- Causes: breakdown in immune tolerance
  mechanisms of tissue injury
    immune complexes, coagulation
  genetic: study families, twins
  environment: sun, drugs

- Women: female hormones
  other: neuroimmunology
  special issues

- Black women: genetic
  access, compliance

- Treatment: innovative; animal models
  patients with SLE

POSTER 6

We need to find out more about the causes of the breakdown of immune regulation; the mechanisms of tissue injury; the genetics of lupus by studying families, especially twins; and how the sun and certain drugs affect lupus.

We need to find out why lupus is so common in women, especially young women. Is it due only to female hormones? Women with lupus need to know whether or not it is risky for them to take oral contraceptives, and when they get older, can they tolerate estrogen replacement.

We need to know why lupus is three times more common in black women than white women. Is it genetic; or socio-economic, such as access to medical care.

We need to test innovative treatments first in animal models and then in women.

Lastly, Mr. Chairman, this year we have major discoveries, as shown on Poster 7, in two forms of that tragic blistering disease epidermolysis bullosa, EB.

[The information follows:]

Epidermolysis Bullosa (EB)

New Developments

- Genes discovered for two forms of EB

- EB Simplex (superficial blisters)
  deficit in genes for keratin
  most abundant protein of
  skin's outer layer

- Classification of EB improved by registry

- Dominant Dystropic EB (deeper blisters)
  defect in gene for type VII collagen
  main component of anchoring fibrils

POSTER 7

In spectacular research, three different NIAMS-supported research teams have found why the skin disintegrates.

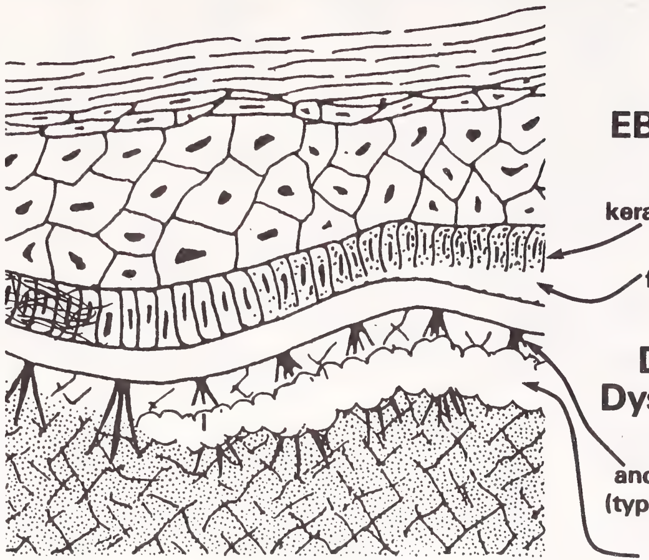
First EB simplex, the most common form, causes superficial blisters when the skin is injured. Two teams of investigators in Chicago and San Francisco proved that the disease is caused by a defect in keratin, which is the most abundant protein produced by cells in the skin's outer layer.

The second is the dominant dystrophic form. By studying large families with this form, a third team in Philadelphia found that this form of EB was caused by the gene for Type VII Collagen, which binds the outer layer of the skin to the deeper layer.

I would like to show you this diagrammatically on Poster 8.

[The information follows:]

Structural Defects in Two Forms of EB



Normal

Abnormal

Epidermis

Basement Membrane

Dermis

EB Simplex

defective keratin filaments

blister formation

Dominant Dystrophic EB

defective anchoring fibrils (type VII collagen)

blister formation

POSTER 8

There is the outer layer of the skin, epidermis, and the lower layer of the skin, the dermis separated by the basement membrane. That is the keratin; the most abundant proteins in the epidermis. The genetic mutation causes a defect in the keratin and that is where the blisters are formed in the simplex form.

The second form of EB occurs at the anchoring fibrils. The mutated gene causes a defect in those anchoring fibrils. Right there, you see the break in the fibrils and that is precisely where the blisters are taking place. We now know the targets; and therefore, we can make additional progress.

Now, I show you a child with EB on Poster 9.

[The information follows:]

Child with EB

POSTER 9

This beautiful child is suffering a great deal. You see that she has scars on her hands. She has bandages on her arms where she is covered with scars from broken blisters. She has some scars, too on her neck that you can see there. We now hope to be able to develop some effectively targeted treatment for EB as a result of this new research.

Overall our research at the NIAMS is devoted and committed to improving the quality of life for our people at all ages, from childhood to maturity.

Mr. Chairman, the fiscal year 1993 budget request for our Institute is $214,929,000. I will be pleased to respond to your questions.

[The statement of Dr. Shulman follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement of the Director
National Institute of Arthritis and Musculoskeletal and Skin Diseases

Mr. Chairman, members of the Committee, it is a pleasure to appear before you today to report on recent research advances and accomplishments of the National Institute of Arthritis and Musculoskeletal and Skin Diseases and to share with you some of our future plans.

As reflected in the name of the Institute, our research programs are rich and diverse. They address the very components of the body--the joints, muscles, bones, connective tissues, and the skin--that are fundamental to human structure, form, and movement. Our programs provide a research agenda and focus for over 100 rheumatic diseases, the many diseases of the musculoskeletal system, and the numerous diseases of the skin.

The research mission of this Institute encompasses a wide number of the most painful, disabling, distressing, and disfiguring diseases and disorders that touch Americans. Take a minute to reflect on your own personal health and the health of your family and close friends. How many times have you or someone you have known been afflicted with low back pain? As we sit here today millions of Americans are experiencing back pain, at an annual cost of $16 billion in medical treatments and disability payments. How many of your mothers or grandmothers have had a broken hip, wrist, or back as a result of osteoporosis and been hospitalized for months? At least 25 million women in this country have osteoporosis; the estimated annual cost to the Nation is $10 billion. Many of us know someone with arthritis who is experiencing the crippling pain of disintegrating cartilage in a knee, hip, or shoulder. An estimated 37 million Americans suffer from arthritis in its many forms. Many of you know a family that has experienced a tragic birth defect. Imagine the emotional and financial toll experienced by the parents of a fragile child born with osteogenesis imperfecta, often called brittle bone disease. It is not unusual for a child with osteogenesis imperfecta to have had over 200 bone fractures by age five. Lastly, picture the frustration and anxiety felt by a mother of a baby born with the blistering disease we know as epidermolysis bullosa, when she cannot hug or physically comfort her crying infant for fear of tearing the baby's skin.

Our research provides hope for these many women, men, children, and families who are living with these and related serious, chronic, and potentially life-threatening diseases. NIAMS seeks to discover the underlying causes of these diseases; to reduce suffering by developing effective treatments; to provide the means to control, cure, and ultimately, prevent these diseases; and to disseminate widely the results of our research. To this end, the Institute conducts and supports basic research in a remarkable range of scientific disciplines, including immunology, molecular biology, genetics, virology, pharmacology, biomechanics, and epidemiology.

Among the Institute's major concerns are the rheumatic diseases. These include such diseases as rheumatoid arthritis, juvenile arthritis, systemic lupus erythematosus, scleroderma, Sjogren's syndrome, Lyme disease, spinal arthritis, and osteoarthritis.

In research on rheumatoid arthritis, over the past decade scientists have gained a clearer understanding of the genetics of this disease, the mechanisms of joint destruction, and the control of the inflammatory process. Advances have helped us to identify those most at risk of developing rheumatoid arthritis. There have been gratifying improvements in therapies, including new anti-inflammatory agents with fewer side effects; new approaches, such as methotrexate, that interfere with basic mechanisms that induce arthritis; and more effective joint replacements that last many years longer than previous ones. Finding the cause of rheumatoid arthritis remains a fundamental goal of both our intramural and extramural researchers today.

Clinical research is also essential. In a major multicenter randomized clinical trial started this past year, the drug minocycline is being evaluated for clinical application and for potential side effects. These studies are ongoing in six locations.

Systemic lupus erythematosus, a serious disease that primarily affects young women, is an inflammatory autoimmune disease in which the immune system mistakenly attacks the body's own tissues. Lupus strikes women nine times more often than it does men; and black women three times more often than white women. NIAMS recently initiated studies on racial characteristics of black women to look for factors that may contribute to their increased risk of developing lupus. In January of this year, NIAMS convened the top researchers in this area to focus on setting a future research agenda to conquer this complex disease. The recommendations developed at this workshop will be used to stimulate new directions for lupus research.

I am happy to report on the tremendous success of the public education efforts and initiatives of the Task Force on Lupus in High Risk Populations. A patient education brochure, "What Black Women Should Know About Lupus," has been sent to a variety of national health organizations and community groups. Over 23,000 copies of the brochure have been distributed in just a few months.

NIAMS-supported investigators are also gaining new insights into scleroderma, another rheumatic disease that predominantly strikes women. Investigators made the exciting discovery this year that the activity of endothelin, a new protein substance produced by blood capillaries, is coupled with two important features of scleroderma--clamping (vasoconstriction) of small blood vessels and the overproduction of collagen. Further investigation of how this protein works offers hope for new forms of treatment against this aggressive, life-threatening disease.

We are educating physicians about another form of arthritis, Lyme disease. The proceedings of a workshop on the Diagnosis and Treatment of Lyme Disease, organized by NIAMS and the National Institute of Allergy and Infectious Diseases, have been distributed to over 65,000 physicians. Lyme disease is an infectious illness that may seriously affect the joints and skin, as well as the nervous system and other parts of the body. In their first year of funding, NIAMS-supported researchers have shown why certain people stricken with Lyme disease may develop chronic arthritis, what parts of the spirochete may be attacked chemically to render it inert, and promising directions for improved diagnostic tests.

Ankylosing spondylitis, one of a family of arthritic diseases called the spondyloarthropathies, which primarily affect spinal joints, can lead to stiffening or fusion of the spine. Researchers have long known that these diseases are strongly associated with the genetic marker HLA-B27. Last year, I reported on the successful reproduction of the important features of this human disease in inbred rats by transgenic transfer of the human gene for HLA-B27. Ongoing research of this transgenic model has shown both (1) that high levels of expression of the gene in the transgenic rats increase the susceptibility of the animals to developing the disease, and (2) that the disease can be reproduced in healthy rats of the same inbred strain by transfer of HLA-B27-expressing bone marrow cells from affected transgenic rats. This research strengthens the case for the importance of the HLA-B27 gene in the development of the spondyloarthropathies.

Equally important to the Institute are diseases and disorders of the musculoskeletal system. These diseases are leading causes of disability among people of all age groups; they include such chronic diseases as osteoporosis, Paget's disease of bone, and inherited diseases such as Marfan syndrome, osteogenesis imperfecta, Ehlers-Danlos syndrome, and muscular dystrophy.

Two important findings have been discovered in understanding the genetic defect causing Marfan syndrome, a serious inherited connective tissue disorder. Scientists have cultured skin cells from patients with Marfan syndrome and found defects in fibrillin, a recently discovered connective tissue protein. Using powerful techniques of molecular biology, teams of investigators reported that the gene for fibrillin is located on human chromosome 15. These discoveries will aid in the diagnosis of Marfan syndrome and may eventually lead to the development of treatment therapies.

NIAMS has significantly intensified its research efforts in osteoporosis and other bone diseases in the past year. New findings on the pathogenesis of Paget's disease have been recently reported. A recent request for research applications on osteoporosis generated 123 responses, resulting in the award of 19 new grants in basic, clinical, and epidemiologic research. Our continuing goal is identifying who is at risk of developing osteoporosis through the earliest detection possible. One specific approach is looking at markers of bone turnover found in blood and urine. These markers may identify persons at risk before osteoporosis is detectable by bone measurement. This would allow intervention to be initiated early in the process.

Past research efforts have clearly demonstrated that the best approach to the prevention and management of osteoporosis is a two-phased lifelong strategy that (1) maximizes the attainment of peak bone mass (reached at about age 35) and (2) thereafter, minimizes hormonal and aging-related bone loss. Research has unequivocally shown that estrogen replacement therapy prevents this bone loss, and recent data confirm that this preventive strategy translates into markedly reduced numbers of fractures. However, the risks and benefits of hormone replacement therapy, specifically in terms of women at risk of breast cancer, are unclear and warrant continued research.

NIAMS has been actively involved in the NIH Women's Health Initiative. The Director of our new Bone Biology and Bone Diseases Branch allocates a significant portion of her time and effort toward this major initiative in women's health. Many of the questions surrounding the risks and benefits of hormone replacement therapy will be addressed through this initiative.

Musculoskeletal fitness and sports medicine are equally important components of our musculoskeletal program. Surveys indicate that almost half the population engages in some form of exercise or sports activity. Physical activity may help preserve and restore bone function and strength, thus aiding in the prevention of osteoporosis. It also improves the efficiency of muscles and allied tissues. However, the less desirable side effect of physical activity is musculoskeletal injury from accidents, inappropriate or excessive activity, or overexertion.

As many of you who have children in sports know, they often go to the emergency room after an injury on the football or baseball field. One NIAMS-supported research team is doing epidemiologic studies of children with sports injuries. Knowing why children get hurt and what can be done to prevent those injuries could help us prevent injury and subsequent disability, and reduce costs to our health care system.

In the area of skin diseases, I am pleased to report significant advances in two forms of the blistering skin disease epidermolysis bullosa. Three NIAMS-supported teams have revealed why the skin disintegrates in these diseases, thus suggesting ways that specific therapies can be designed. Moreover, researchers are using this new knowledge to carry out wider studies in such areas as wound healing and skin aging.

In the treatment of recalcitrant psoriasis, a clinical trial testing graded doses of cyclosporine has demonstrated that cyclosporine therapy leads to a rapid and thorough clearing of the red, scaling lesions. An initial low dose of 5 mg per kg per day was shown to be safe and effective.

Alopecia areata, a common disease of the hair follicle, is another important area of skin research for our Institute. The social and emotional impact of this disease, which causes those affected to lose hair on the head and elsewhere, can be devastating for young children and women in particular. NIAMS looks forward to supporting research in response to a recent program announcement on the molecular and structural biology of hair and its diseases with special reference to alopecia areata.

I am also pleased to report that the Laboratory of Skin Biology in our intramural program has expanded to carry out clinical genetic research on patients with scaling skin diseases and to design animal models for these disorders. In addition, our intramural program offers unique training opportunities, such as fellowships in pediatric rheumatology and biomechanics.

In closing, I want to tell you about a new endeavor by the Institute to pursue opportunities for clinical investigations and clinical trials. In four separate workshops, we convened experts in arthritis, skin diseases, bone diseases, and musculoskeletal disorders to discuss the need for clinical studies in these areas. Each workshop has identified specific studies that should be addressed over the next 10 years.

Mr. Chairman, the FY 1993 budget request for this Institute is $214,929,000. I will be pleased to answer any questions you may have.

SHULMAN, DR. LAWRENCE E.
Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases,
National Institutes of Health

July 25, 1919, Boston, Massachusetts

Education: Harvard University, A.B., 1941; Yale University Graduate School, Ph.D., 1945; Yale University School of Medicine, M.D., 1949.

Professional History: 1949-50, Intern, Medicine, The Johns Hopkins Hospital, Baltimore, Maryland. 1950-51, Ayerst, McKenna and Harrison Fellow in Endocrinology, The Johns Hopkins University School of Medicine. 1951-52, Vernon D. Lynch Fellow in Internal Medicine, The Johns Hopkins University School of Medicine. 1952-53, Assistant Resident, The Johns Hopkins Hospital. 1954-present, Physician, The Johns Hopkins Hospital. 1955-75, Director, Connective Tissue Division, Department of Medicine, The Johns Hopkins University School of Medicine. 1960-66, Physician-in-Charge, Arthritis Clinic, The Johns Hopkins Hospital. 1956-67, Physician-in-Charge, Connective Tissue Clinic, The Johns Hopkins Hospital. 1966-69, Physician-in-Chief, Division of Chronic and Community Medicine, The Baltimore City Hospitals, Baltimore, Maryland. 1970-73, Associate Professor of Medical Care and Hospitals, The Johns Hopkins University School of Hygiene and Public Health. 1964-present, Associate Professor of Medicine, The Johns Hopkins University School of Medicine. 1976-80, Acting Associate Director for Arthritis, Musculoskeletal, and Skin Diseases, National Institute of Arthritis, Metabolism, and Digestive Diseases. 1980-83, Associate Director, Arthritis, Musculoskeletal and Skin Diseases, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases. 1983-1986, Director, Division of Arthritis, Musculoskeletal, and Skin Diseases, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases. 1986, Acting Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases. 1987-present, Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases.

Professional Organizations: American Association for the Advancement of Science, American College of Physicians, American Federation for Clinical Research, American Rheumatism Association (President, 1974-75), American Society for Bone and Mineral Research, The Arthritis Foundation, Brazilian Society of Rheumatology, Carla Curzio Neapolitan Society, Lupus Foundation of America, New York Academy of Science, Pan American League Against Rheumatism (President, 1982-86), Society for Clinical Trials, Sydenham Society, Society for Investigative Dermatology.

Honors, Awards: Senior Investigator Award, The Arthritis Foundation, 1957-62. Pemberton Memorial Lecture, 1963. Fellow, American College of Physicians, 1967. Wallace R. Graham Memorial Lecture: Toronto, 1973. The Heberden Medal for Research in the Rheumatic Diseases, Heberden Society, London, 1975. Distinguished Service Award, The Arthritis Foundation, 1979. Honorary Member, Brazilian Society of Rheumatology, 1980. Honorary Member, Chilean Society of Rheumatology, 1981. Knowles Lecture: San Francisco, 1982. Honorary

Member, Costa Rican Association of Rheumatology, 1984. Honorary Member, Australian Rheumatism Association, 1985. The Public Health Service Superior Service Award, 1985. National Lupus Hall of Fame, 1986. Honorary Member, Swiss Society of Rheumatology, 1987. Elected Master, American Rheumatism Association, 1987.

NATIONAL RESEARCH PLAN

Mr. NATCHER. Thank you, Dr. Shulman.

Now, Doctor, for the last several years we have discussed your Institute's research plan. Have you now finished the plan, Doctor?

Dr. SHULMAN. The research plan is coming along beautifully, sir. The answer is, we are almost finished with the plan.

As you know, about a year ago, we had this marvelous task force consisting of 14 different science panels: five in the science areas of our Institute—arthritis, muscle biology, bone biology and bone diseases, musculoskeletal diseases, and skin diseases; and nine cross-cutting panels. A tremendous amount of material was generated by this task force. I will give you the number of pages as it stands right now. There are a total of 1,334 double-spaced pages full of recommendations. The status is that nine of them are completed or in the final revisions. The others are in the advanced stage of preparation.

What we have done is taken the first drafts of each of these 14 panels and, as stipulated in our legislation, we have presented them to our National Advisory Council and our National Advisory Board. It took two meetings of each of these advisory bodies to review the plan. Suggestions were made. These were sent back and reviewed by the co-chairpersons and are now incorporated in the plan. So this is the current status. We hope to be able to complete the process by this summer.

PROGRESS OF RESEARCH

Mr. NATCHER. Many of the diseases within your jurisdiction have been under study for about 40 years. Would it be fair to say, Doctor, that progress has been made in the treatment area, rather than in determining the cause or cure for these diseases?

Dr. SHULMAN. There has been a tremendous amount of advance made in the treatment area. There has been an equally impressive and even more hopeful progress in disease mechanisms.

I presented advances to you in terms of rheumatoid arthritis, that is a beautiful example. The same is true of lupus. The treatments developed are the results of the finding of potential causal pathways in each disease. In lupus, the immunotherapy is based upon the elegant immunological research that has been carried on in lupus itself.

I think we are beginning to make some real headway in basic causes, for example, finding a gene for one form of osteoarthritis. Basic research is now beginning to pay off, as well as the advances we have made on the treatment side.

RESEARCH PRIORITIES

Mr. NATCHER. Your Institute's research mission is very broad, Doctor; some areas must present more research opportunity than others. What are the one or two areas of research that would be the most cost effective to expand?

Dr. SHULMAN. Well, that is very hard to answer, sir, because there are so many. We have developed our list of priorities for you and for this Committee.

We have priorities in two different methods. We have priorities by disease area and priorities in general for the Institute. If I may first speak to the priorities in general, we need to expand our knowledge of genetic predisposition to diseases within the research mandates of NIAMS.

Second, we need to approach the use of biologics and molecular biology to control disease.

Third, we need to expand our knowledge of the source of race and sex distribution in the epidemiology of diseases.

Four, we need to move forward and expand our portfolio of clinical investigations and clinical trials.

With respect to the diseases themselves, Mr. Chairman, the following diseases are of vital importance to us, as well as the others: rheumatoid arthritis, lupus, osteoporosis, Lyme disease, musculoskeletal fitness, sports medicine, certain types of molecular genetic diseases involving the skin, and expansion of the NIAMS intramural program.

ORPHAN DISEASES

Mr. Natcher. Your Institute is responsible for a variety of diseases, some common and some very rare. When you are allocating research dollars, do you consider the prevalence of a disease?

Dr. Shulman. To some degree, but by no means is that ruling in terms of what we do. That does not dominate our thinking.

We have a keen interest in the orphan diseases, the rare diseases. They are just so terrible. We showed you EB. Osteogenesis imperfecta, is a terrible inherited disease in which young children may have as many as 200 fractures by the time they are one year old. That is pretty compelling and gets pretty high on our research agenda.

There are obviously considerations in terms of the overall health and economic burden to the Nation, so that some diseases, such as osteoporosis, which costs the Nation $10,000,000,000, are getting such high attention, as shown in my presentation to you this morning.

SPECIALIZED RESEARCH CENTERS

Mr. Natcher. We understand you are recompeting your specialized centers this year. Will you award the same number of grants in each of the program areas as in the past?

Dr. Shulman. This is our plan, yes. In each of the three diseases of rheumatoid arthritis, osteoarthritis, and osteoporosis, nine in all.

Mr. Natcher. How many applications have you received?

Dr. Shulman. We have received four applications each in osteoporosis and osteoarthritis, and five in rheumatoid arthritis, including the three currently being funded.

AVERAGE GRANT COST

Mr. Natcher. How do you maintain the Institute's average grant cost below the NIH average?

Dr. Shulman. I wish I could say that was by design, sir, but it is not. It happens to be what is received by our Institute.

Our Institute is $30,000 to $35,000 less than the average cost of the NIH. I think the FY 1992 average for NIH is $225,000; I think the average in the past two or three years for the NIAMS has been ranging from $180,000 to $200,000. The projection for the FY 1993 request is just under $200,000 average cost.

CLINICAL TRIALS

Mr. NATCHER. Your Institute has a small clinical trials program. Is more basic research needed, Doctor, before you can expand your clinical program?

Dr. SHULMAN. No, sir. We have a lot of clinical trials that need to be carried out. We have a list with us right here of 16 additional new clinical trials that everyone has recommended that we carry out. We have costed these out to be something in the order of $12,700,000.

We would support clinical trials by different mechanisms, contracts, cooperative agreements, research grants—but our contract line is lower than the NIH average. Our contract line is 1.9 percent of our Institute's budget, compared to something between 7 and 8 percent for the NIH as a whole.

Mr. NATCHER. If you had the flexibility, would you transfer money from other mechanisms to clinical trials?

Dr. SHULMAN. That is a tough question to answer. We are so constrained in so many areas. We agree the research project grants are at the highest level of our agenda. We would like to be in a better situation to be able to afford to do those clinical trials.

INTRAMURAL RESEARCH

Mr. NATCHER. Less than 8 percent of your budget goes to inhouse research, compared to more than 11 percent NIH-wide. Are you comfortable, Doctor, with the size of your in-house program?

Dr. SHULMAN. We are very pleased with the quality of the program. We are not comfortable with that percentage at all.

When we were first created, Mr. Natcher, we were allotted two units, a branch and a laboratory, that amounted to 5.5 percent of our budget. We compared that to the average at NIH, which was approximately 11 percent.

Also, you asked in report language that a report for the expansion and future development of the intramural research program be developed. That was done in 1988, and has been submitted to the Congress. That report recommended that we have six new laboratories and work on four new major diseases. We have been working toward that goal.

In the last year, we created two new units, a Laboratory of Structural Biology and the Laboratory of Skin Biology. They are at the top of the NIH agenda in terms of the types of research they are doing, and we are very pleased with it.

We also urgently would like to create a new Laboratory of Connective Tissue Biology. We have lots of plans for the further development of our intramural programs.

Mr. NATCHER. Mr. Stokes, I yield to you.

LUPUS

Mr. STOKES. Thank you, Mr. Chairman.

Dr. Shulman, I am sure I speak for both Mr. Pursell and myself when I say we are very pleased with your response to our concerns about lupus; and the presentation you made this morning is certainly very, very impressive. We want to talk about it a little bit more, though.

It is my understanding that men also get lupus, but that 9 out of 10 percent who get it are actually women; is that correct?

Dr. SHULMAN. Yes, sir.

Mr. STOKES. How many women would you say, in the United States, have lupus?

Dr. SHULMAN. We have done an in-depth analysis of what that might be. The studies that have been done not only in this country, but around the world, have reported somewhere between 10 and 50 per 100,000 population, which if you translate the upper one of taking 50, that would mean that we would have something in the order of 130,000 to 140,000 women in the United States.

Those were obtained using rather rigid criteria for the diagnosis of lupus, so it is quite possible that there are many more people with lupus than are indicated by these classification criteria. I would say there are somewhere between 150,000 and 500,000 people with lupus in the United States.

Mr. STOKES. So, we understand the disparity with reference to African American women having lupus. How do you categorize it?

Dr. SHULMAN. This is a very important subject. We are trying to look into all aspects of it. There are active studies going on that come up with different points of view. We need to clarify it.

For example, what we are trying to do is look at the genetics. For example, there is a wonderful opportunity in the Caribbean—you know, we have the Latin American-Caribbean Initiative at NIH. Dr. Lockshin, who is the director of our Extramural Program, and Ms. Reva Lawrence have been working actively with scientists in the West Indies and the university there to develop some exciting research initiatives.

On one island in the Caribbean, half the population is of African-American origin and the other half is East Indian. This ethnic distribution provides a wonderful opportunity to look into the question of genetics versus environment. Some recent lupus studies have indicated there are socioeconomic factors involved, like access to health care. Another factor would be whether they have proper compliance with drugs—a whole host of efforts to pursue. So we are looking into these factors and want to expand our research in this arena.

Mr. STOKES. You indicated in your presentation that because of the research that is now being done in this area that it appears that persons with lupus are living longer. What is the rate of mortality; so that we can put it in the proper context?

Dr. SHULMAN. Mortality is expressed in survivorship, how many people are surviving. It is a curve that the insurance company uses.

The figures are that over 90 percent of women with lupus are surviving 10 years after diagnosis. It is even longer because there is an interval between the onset of the disease and the diagnosis.

Mr. STOKES. How much funding are we putting into this area in your fiscal year 1992 and 1993 budgets?

Dr. SHULMAN. In lupus research, in 1992, it is $12,566,000; in 1993, $13,221,000. That is a 5.2 percent increase we are projecting for this year.

Mr. STOKES. In terms of the research efforts that you are involved in, do you have any outside institutions that are working with you on the problem in terms of research? For instance, are you utilizing the historically black colleges and universities to any degree?

Dr. SHULMAN. We are going to move into high gear on that. I am pleased to report that Dr. Vivian Pinn, Director, Office of Research on Women's Health, is going to be working very closely with us. She is a great asset to us.

We have had conversations on how we are going to collaborate on lupus research. She has arranged for me to give a talk at the National Medical Association and work with historically black colleges. We intend to pursue this to the fullest.

NEUROSKELETAL RESEARCH

Mr. STOKES. A doctor has estimated that about 200,000 persons in the United States have persistent paraplegia or quadraplegia caused by injury to the spinal cord, and about 800,000 persons are paralyzed each year. Total health care costs average about $170,000,000,000 annually.

Last year, language was placed into the House report urging the establishment of a neuroskeletal science center to study neurological and skeletal disorders. Have we done anything about that at all?

Dr. SHULMAN. We are talking with the people in the Neurology Institute about how to combine our forces.

Mr. STOKES. Can you tell us currently what type of research has been done in this area?

Dr. SHULMAN. We are doing research on how one combats muscle weakness and on the development of new prosthetic arms that more closely resemble the motion and forces of natural arms. Our side of this, which is on the muscle side, is what we are doing. We have a whole program working in the area of muscle weakness and methods to combat it. Actually, we are even working with the people at NASA to try to combat the muscle weakness that occurs in space, as we are concerned with that aspect of the neuromuscular deficit that would occur under those instances. Also, we fund research on the strength of the spinal bone and connective tissues that relates to spinal injury prevention. The Neurology Institute works on the neurology side of it.

Mr. STOKES. How much funding are we providing?

Dr. SHULMAN. In terms of muscle function, we estimate $16,563,000 in FY 1992 to go up to $17,656,000 in FY 1993 in muscle function; muscle diseases, over $5,000,000; muscle development and regeneration, $2,000,000, in that arena. In neurosciences research, we have $1,959,000 in FY 1992—that is neurosciences in this Institute. You can see we are more on the muscle side than the neurosciences side.

Mr. Stokes. Is there a reason why?

Dr. Shulman. The Neurology Institute is devoted to neurology disease. We meet at the synapse between the nerve and the muscle. It is acetylcholine that divides one Institute from another.

RHEUMATOID ARTHRITIS

Mr. Stokes. I guess I will just leave that alone.

Let me ask you about rheumatoid arthritis, which I understand afflicts over 2,000,000 Americans. To what extent do we understand that genetic immunologic and environmental factors relate to this disease?

Dr. Shulman. That is a good question. On the genetic side, there is a very strong association in adults with rheumatoid arthritis with a genetic determinant called DR-4. In children, the determinants are different. There are two kinds in children; each of the two kinds has a different genetic determinant. So the genetics for rheumatoid arthritis are not simple. There is more than one gene involved in the production of rheumatoid arthritis.

I described immune processes before you came, sir. There is an amazing category of immune responses. We are getting more and more sophisticated about understanding the way the immune responses work and how they then destroy the cartilage in the joint.

In terms of the environment, there are some intriguing things taking place. It has been shown certain chemicals in bacterial cell walls produce arthritis in experimental animals.

We have not yet identified a bona fide single organism that we can say can cause rheumatoid arthritis, but there is a continuing search for such, and we are going to pursue that further. So it is the combination—genetics, immune effects, and environment that affect rheumatoid arthritis.

Mr. Stokes. Thank you.

DOWNWARD ADJUSTMENT OF GRANTS

Mr. Natcher. Doctor, how are you handling the issue of downward adjustment of grant awards in 1992 and 1993?

Dr. Shulman. We call them "budget adjustments." The budget adjustments are done on an individual basis. We are supposed to stay away from the word "downward," I think. The budget adjustments, on the average, for our Institute are overall about 10 percent for both years, 1992 and 1993. In 1991, they were 8.2 percent.

BUDGET FLEXIBILITY

Mr. Natcher. Aside from not having as much funding as you would like, Doctor, what is the most serious systematic problem with your budget?

Dr. Shulman. We, of course, do the very best we can with what we are allotted. I don't think there is one most-serious difficulty with the budget. I do think, from a personal standpoint, that there is not as much flexibility as would be desirable to take advantage of special initiatives.

Research project grants are our highest priority, and we agree with that. But at the same time, what happens is that there is no give, and, in fact, some decreases in all other research mechanisms. So I would say, from my personal standpoint, there is less flexibility to take care of special opportunities.

OSTEOPOROSIS

Mr. Natcher. Do you expect to receive any grant funds from the Office for Research on Women's Health to study osteoporosis, Doctor?

Dr. Shulman. I would think, yes, we would.

Dr. Pinn has just started to carry on discussions with all the Institutes and Centers. She has selected ours to be among the first of those to meet. I am sure that we will be doing some collaborative work, and that they would wish to support research in both these areas, sir.

Mr. Natcher. Since the women's health study is supporting major research on osteoporosis, will this free up money in your budget which you can allocate to other activities, Doctor?

Dr. Shulman. No, sir.

Mr. Natcher. In response to congressional interest, you are awarding a contract for an osteoporosis resource center?

Dr. Shulman. Yes, sir.

Mr. Natcher. What is the main purpose of the center who is the intended audience, Doctor?

Dr. Shulman. This resource center is to serve as an area for expert public information and public education concerning osteoporosis, Paget's disease, osteogenesis imperfecta, and other bone disorders. A whole host of important activities will be carried out by this resource center, for which we are having a competitive contract. This resource center will reside outside the government, as you know, and will be awarded following a full and open competition. I think that this center will give all of us the opportunity to highlight information and give information to both the public and professionals.

Mr. Natcher. How much funding will you allocate for the center in 1992 and in 1993?

Dr. Shulman. We will fund the center in 1993. We will not be able to fund it before that because the competition will be completed in the fall. We estimate it to be in the area of $750,000.

DISEASE REGISTRIES AND CLEARINGHOUSES

Mr. Natcher. How many diseases registries or clearinghouses are currently operated by your Institute?

Dr. Shulman. There is one clearinghouse, an excellent clearinghouse. We have one registry, the registry for epidermolysis bullosa. This is a very successful registry.

It started off with a budget in 1986 of a little over $500,000. We are recompeting it now and it is being actively negotiated. It is now in the area of approximately $1,000,000 a year for the registry.

Mr. Natcher. Should the Committee resist pressures to further expand the number of disease-specific registries at NIH, Doctor?

Dr. Shulman. Sir, I find it very difficult to answer that question directly. I don't have any experience with other registries at NIH, but certainly the experience from this registry has been very helpful and very productive. I think, however, they are proving to be costly.

We are wondering about the advisability of creating rosters—in which you can gather lists of patients on a national basis—rather than supporting more sophisticated research activities as a result of that collection of cases.

LYME DISEASE

Mr. Natcher. Doctor, what progress can you report on finding better diagnostic tools for Lyme disease?

Dr. Shulman. You will notice that in the booklets that I prepared for you there is a poster on Lyme disease, but I thought I would be speaking too long, so I eliminated it from my presentation. In the first place, Lyme disease continues to increase. There was a hope last year that the prevalence was going down. But it is going up again.

The number of cases in 1991, as reported by the Centers for Disease Control is 9,440 new cases. We have discovered the cause of this disease, the borrelia burgdorferi, and how you get it, from the tick bite.

We still have problems with the diagnosis and treatment of Lyme disease, as we discussed with you last year. Therefore, a year ago we and the National Institute of Allergy and Infectious Diseases held a state-of-the-art workshop for diagnosis and treatment of Lyme disease. The proceedings were published, and there is a copy of them on the desk. We have distributed the proceedings to over 65,000 physicians, giving them the latest information developed by a representative group of experts on both sides for diagnosis and treatment.

We put out, at the same time, Mr. Chairman, a request for applications for diagnosis and treatment of Lyme disease. We have funded nine new research projects because of that request. This year we have had progress in improved diagnostic methods.

First, there are better ways to culture the skin and other specimens. By use of the PCR, the polymerase chain reaction, we have improved the ability to detect the organisms. That is a triumph in biology, because of PCR's ability to detect the organism in the blood, urine, and spinal fluid.

In March, in the Journal of the American Medical Association reported, researchers studied a group of patients with early Lyme who had multiple skin lesions indicating that it had spread throughout the body. Some of those patients had headache and fever.

The question was—has that organism, the bug, gone into the spinal fluid and the brain? When you examine the spinal fluid, researchers were not able to pick up an antibody indicating there was disease in the brain. But the PCR reaction did detect evidence that there was disease in the brain.

The implications are that you should give more intensive intravenous treatment if you are able to pick up the disease that early. It is very wonderful early diagnosis and treatment.

We need more research on the later forms of the disease, but prevention is the key. Education is important, how to protect yourself in the summer. We no longer lead the good life in the summer, if you live in Lyme, Connecticut. We also have some promising work on prevention which also includes the development of a vaccine.

Mr. NATCHER. What are the prospects for developing a Lyme disease vaccine?

Dr. SHULMAN. I think it is promising; there are vaccines that have been produced in mice and hamsters and in dogs. The experts feel that they have a fairly good chance of producing one in humans, but they think that it is going to be difficult to do so.

MUSCULAR DYSTROPHY

Mr. NATCHER. What progress has been made in the last year in developing vaccine therapy for muscular dystrophy, Doctor?

Dr. SHULMAN. There has been remarkable progress in terms of characterizing, two forms of muscular dystrophy. One we have been reporting for the past three or four years is Duchenne's type of MD, which is fatal to boys and it has been discovered by the work of Dr. Kunkel and others, that the absence of a protein called dystrophin causes the muscular dystrophy.

The gene has been identified, the severity has been located to the defect in the dystrophin gene, and there has been a full-length replica of this dystrophic gene. It was a great advance, prize-winning research.

There has also been very recent great progress in myotonic dystrophy that affects adults. There is a distribution of the genome that causes this. The severity is found to increase in successive generations; we need to find out what the basic reason for that is. There is great progress in both areas.

In the area of gene therapy, I know of no breakthroughs in that arena.

ALOPECIA RESEARCH

Mr. NATCHER. For the first time, you have issued a program announcement on alopecia research. Are you getting a good application response, Doctor?

Dr. SHULMAN. It is encouraging, sir. About two years ago, we had nothing, no grants. We held a workshop which turned out to be really quite interesting. The findings of the workshop were published in the "Journal of Investigative Dermatology", and we then put out a request for applications. We have three excellent new grants this year in alopecia that we did not have before.

I would like to tell you another story about one of the scientists who submitted a grant application for research on alopecia from New York University; his grant was just a bit above the pay line. He had decided that he was going to give up research. So he rented an office, was about to set up a practice and leave research when he got an announcement that he was offered a Shannon Grant. He went back to the head of his department and asked if he could have his lab back, and they said yes. Now he has gone back into research. He is one of our new grantees.

Mr. NATCHER. How much are you likely to put into this area in 1992 and 1993?

Dr. SHULMAN. About $200,000.

Mr. NATCHER. Thank you.

I yield to Mr. Stokes.

MARFAN SYNDROME

Mr. STOKES. I want to talk about Marfan syndrome. Is this a very serious disease?

Dr. SHULMAN. Marfan syndrome is inherited. It is the most common of the inherited connective tissue diseases.

It is a dramatic and tragic disease, which produces skeletal defects with loose joints, that is why we are interested in it. It produces a terrible weakness of the aorta and dislocation of the lens in the eye. People who have it are very tall with long extremities—long wing-spread, if you wish. A lot of research was being done, but we never knew what the basic defect was.

In 1986, a new protein was discovered in the connective tissues cells, fibrillin. The discovery of the gene for fibrillin was reported in the July 25 issue of Nature—I know that because it is the date of my birthday. This issue has on the front cover a picture of Abraham Lincoln. There were three reports on Marfan syndome in which they located the gene for fibrillin on chromosome 15.

One of the most notable cases is Flo Hyman, who you remember was the star volleyball player on our Olympic team, who collapsed and died on the court as a result of the rupture of her aorta.

Dr. Gott at Hopkins has developed a surgical way to strengthen the aorta if people develop a weakness there.

Mr. STOKES. How many Americans do you believe are affected by this disease?

Dr. SHULMAN. I really don't know. I think it is in the thousands.

OSTEOPOROSIS

Mr. STOKES. I was reading in your budget document about osteoporosis. One of the interesting factors about it is that it is diametrically opposite the usual circumstances with reference to diseases, where African American women are more affected. This is one where white women are more affected than African American women; is that correct?

Dr. SHULMAN. That is correct. It is very interesting that it is actually the case for both black women and black men. As background, we all build up bone until the age of 35, and it is all down hill thereafter. We start to lose bone.

Research has shown that African American people build up more bone than white people by age 35. As a result the bone density in African American people is greater than in white people. There is research that indicates that this does not start in childhood but there is a spurt in adolescence, after puberty, in which the African American people develop much more bone.

We don't know why that is. By the way, it is also good to be fat. Being fat is good for your bones.

Mr. STOKES. What does that do to cholesterol?

Dr. SHULMAN. It is bad for cholesterol.

SKIN CANCER

Mr. STOKES. Let me ask you this: Many minorities believe that they cannot get skin cancer, particularly African Americans.

Is this true or do they have less of an incidence of skin cancer than other groups?

Dr. SHULMAN. I have heard that is the case.

I will find out for you but I don't know.

[The information follows:]

SKIN CANCER

It is true that certain minorities have a lower incidence of skin cancers of certain types than do Caucasians. This is true for the sun-related forms of basal cell and squamous cell cancer and for melanoma as they relate to African Americans and Asian Americans and to a lesser degree, hispanics. The incidence is lower, but these cancers do occur in these individuals as a result of sum exposure. With respect to skin cancers that are not related to sun exposure, such as cutaneous T-cell lymphoma and certain sub-groups of basal and squamous cell cancer and melanoma, here the incidence seems to be the same for African Americans, Asian Americans, Hispanics and Caucasians. Overall, however, since the sun-related forms of skin cancer in the United States represent the majority of all skin cancers, it is true that most minorities have a lower incidence of skin cancer when skin cancers are considered as a whole.

OFFICE OF MINORITY HEALTH

Mr. STOKES. Let me ask you this: To what extent does your office work with the Office of Minority Health?

Dr. SHULMAN. We will be working with them. They are very busy developing their agenda on all scores.

We will be developing an agenda with them on lupus. We work with the Office of Minority Health, not only in the NIH but within the Department at the Assistant Secretary's office on lupus.

Dr. John Ruffin, the Associate Director for Minority Health, is keenly interested in our lupus efforts. We need to do something in the area of vitiligo as well, but we have not gotten to that as yet.

Mr. STOKES. Thank you.

Thank you, Mr. Chairman.

Mr. NATCHER. Dr. Shulman, we want to thank you and your associates for appearing before our Committee at this time on behalf of your budget request for the fiscal year 1993.

Thank you very much.

[The following questions were submitted to be answered for the record:]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

Mr. Natcher: What is the cost in 1992 and 1993 of the arthritis, musculoskeletal and skin diseases information clearinghouse?

Dr. Shulman: The cost of the NIAMS clearinghouse for FY 1992 is estimated to be $420,000. For FY 1993 the estimate is $450,000. We also plan to award a contract for approximately $750,000 for the Resource Center on osteoporosis and related bone disorders in FY 1993.

Mr. Natcher: Identify estimated 1991-1993 spending on the following: Osteoporosis, EB, Marfan's syndrome, lupus, osteoarthritis, rheumatoid arthritis, scleroderma, Lyme disease, muscular dystrophy, psoriasis, and alopecia areata.

Dr. Shulman: The following table identifies the NIAMS actual FY 1991 obligations and FY 1992 and FY 1993 estimates.

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES
(Dollars in thousands)

	FY 1991	FY 1992	FY 1993
Osteoporosis	37,566	39,350	41,822
Epidermolysis bullosa	3,332	3,484	3,708
Marfan's syndrome	659	688	736
Lupus	11,959	12,566	13,221
Osteoarthritis	9,515	10,184	10,541
Rheumatoid arthritis	16,403	18,004	18,504
Scleroderma	2,144	2,285	2,395
Lyme disease	3,424	3,574	3,826
Muscular dystrophy	1,176	1,234	1,304
Psoriasis	2,927	3,047	3,234
Alopecia areata	186	183	196

Mr. Natcher: How do you intend to spend the $500,000 you received by transfer from the Cancer Institute in 1992?

Dr. Shulman: The NIAMS intends to fund competing research grants with the additional $500,000 for research in skin cancer and bone cancer.

Mr. Natcher: Identify the number and type of centers funded in 1992 and in the 1993 budget.

Dr. Shulman: The following table identifies the number and type of centers that are being funded in FY 1992 and FY 1993.

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES
(Dollars in thousands)

	FY 1992		FY 1993	
	NUMBER	AMOUNT	NUMBER	AMOUNT
Specialized Centers of Research (SCORS)	9	$ 7,544	9	$ 7,693
Comprehensive Centers (MACS)	14	13,436	14	12,868
Center Core Grants	5	1,981	5	2,400
TOTAL	28	$22,961	28	$22,961

Mr. Natcher: Does your Institute do any research in the area of burn treatment?

Dr. Shulman: NIAMS through its Skin Diseases Program supports research on healing of skin wounds of all sorts, both burns and other forms of chronic and acute skin loss. We also support much basic research on the steps involved in wound healing and in epidermal regeneration and differentiation. Most of this research is directed at a basic understanding of the wound healing process as applicable to all wounds, both acute wounds, such as burns, and chronic wounds, such as decubitus and stasis ulcers. Some of this research is directly applicable, and has been used in the development of burn treatment procedures, such as artificial skin development. However, the bulk of the support of research in the healing of skin wounds is in the basic understanding of the process, which will then have application not only to burn treatment, but to all forms of wound healing in the skin.

LUPUS

Mr. Stokes: You also indicated last year that the Institute planned to pursue lupus research in Africa, in order to determine if the genetic, ethnic, or not. What progress have you made in supporting research activities in Africa?

Dr. Shulman: As part of the Caribbean initiative, NIAMS has met with members of the Caribbean Commonwealth Medical Research Council and has held workshops concerning the genetic and ethnic determinants of lupus, particularly in African Americans. Because there has been considerable British Commonwealth interest in the Caribbean in the past, British investigators have participated in the deliberations. There are now ongoing discussions about establishing, through England, parallel studies that will look at Africans in Nigeria, African Americans in the United States, African Americans in the Caribbean, immigrant African Caribbeans to England, and immigrant Africans to England. Researchers in Nigeria, England, and various Caribbean islands and the United States are now identified. We anticipate that grant applications will be received in Fiscal Years 1992 and 1993 and will be funded in Fiscal Year 1993 and Fiscal Year 1994.

Mr. Stokes: In addition to possible biological factors, what do we know about the socioeconomic variables that are at work?

Dr. Shulman: Studies recently published suggest that the high attack rate of lupus in African/American populations may be more a function of socioeconomic factors than of race. Specific components that have been suggested include access to medical care, quality of medical care, compliance with medical care, and influence of other complicating medical problems such a hypertension. The cross-cultural studies in which socioeconomic status is constant, such as can be performed in the Caribbean populations, may help to sort out the relative roles of genetics and socioeconomic variables.

MARFAN SYNDROME

Mr. Stokes: Marfan syndrome occurs when there is a defect in the connective tissue. The Olympic volleyball player Flo Hyman died of this disease. What extent are the current methods of diagnosis and therapy?

Dr. Shulman: Diagnosis of Marfan syndrome is straightforward when all of the manifestations of the disease are present: tallness, long fingers, breastbone deformities, dislocated ocular lens, nearsightedness, aortic regurgitation, and heart valve dysfunction -- mitral valve prolapse. However, physicians seldom encounter any one patient with all of these problems. Signs that arouse suspicion of Marfan syndrome include (1) a family history of the disease and (2) tallness plus any two of the other factors listed above. The disease can be diagnosed with the aid of echocardiography, a form of ultrasonic imaging of the heart.

Since the late 1960s, physicians have been using beta-adrenergic blockers to treat patients with Marfan syndrome. The object is to reduce the abruptness of ejection of blood from the heart, thus lessening the physiological pounding on the ascending aorta; the rupture of which caused the death of Flo Hyman.

About 20 years ago a composite graft operation was introduced, in which the aorta and aortic valve are replaced by a synthetic tube that has an artificial valve sewn into it. This operation--in its various modifications that have occurred over the years--has been highly successful in treating the syndrome.

RHEUMATOID ARTHRITIS

Mr. Stokes: The disease affects women more than men, is that correct?

Dr. Shulman: The adult form of rheumatoid arthritis affects women approximately three times as frequently as it affects men.

Mr. Stokes: Do we know why?

Dr. Shulman: The reasons why rheumatoid arthritis is more frequent in women than in men is not known at this time. One hypothesis is that women and men are equally exposed to the agent that causes the disease, but that women have a different form of immune system than do men and that the differences may be accounted for by hormones acting on the immune system. The relief of the illness during pregnancy and its recurrence when pregnancy concludes is one of the bits of evidence supporting this theory.

Mr. Stokes: To what extent are minorities affected compared to whites?

Dr. Shulman: We know of no minorities that suffer disproportionately from rheumatoid arthritis when compared to whites--except for the Pima Indians, a unique tribe living in Arizona. The Pimas have an incidence that is tenfold higher than in Caucasian populations. The Institute is currently supporting an epidemiologic project in Arizona aimed at finding out why this is so.

OSTEOARTHRITIS

Mr. Stokes: Osteoarthritis, a degenerative joint disease caused by progressive deterioration of cartilage and overgrowth of bone, is the most common form of arthritis, affecting almost 16 million Americans. To what extent do we understand the factors which lead to initial deterioration and rapid degeneration?

Dr. Shulman: There have been several recent advances in our understanding of osteoarthritis. In at least some cases we now know that the gene that produces collagen -- the basic chemical constituent of cartilage -- is faulty. We know that certain mechanical factors, including work activity and excess weight in the knees cause cartilage to wear out early. We also now understand how certain enzymes within the joint destroy the cartilage and in part, how to stop the action of these enzymes. Each one of these new factors has suggested a logical treatment, and these treatments are now being considered for testing.

Risk factors for initiating osteoarthritis include obesity, repeated knee bending activities, and injuries; such as, cruciate ligament and meniscus tears in the knee. There is improved knowledge of biomechanical factors; such as, anatomic fit of the adjacent bones, strength of supporting connective tissues, and material properties of the component tissues that affect joint stability and may predispose an individual to osteoarthritis.

Mr. Stokes: What progress has been made in the area of diagnosis and therapy?

Dr. Shulman: Measurements of products released into the blood in the joint fluid from degenerating cartilage can now be made. There is some hope that these measurements will let physicians make better decisions about when to initiate treatment. Treatment itself has improved in the past decade leading to better pain control and better joint replacement. New forms of therapy, based on protection of the cartilage from wearing out, and the future forms of therapy based on helping cartilage regrow are being sought at this time.

Recent clinical studies have demonstrated that analgesic, pain-relieving agents, such as acetaminophen, are at least as effective as agents with analgesic and anti-inflammatory properties, such as ibuprofen, in the treatment of osteoporosis of the knee. This study has implications for the safety and cost of treatments for this condition.

Mr. Stokes: Does this disease affect women more than men?

Dr. Shulman: When the various factors of weight, injury history, work history, and other concerns are taken into account, the disease affects both men and women equally. The only exception to this is possibly in osteoarthritis of the knees in which women are slightly more frequently affected than are men.

Mr. Stokes: Minorities more than whites?

Dr. Shulman: No, the disease does not appear to affect minorities more than whites.

Mr. Stokes: What level of funding supported research in this area in FY 1992?

Dr. Shulman: The NIAMS is expecting to fund $10,184,000 for osteoarthritis in FY 1992.

Mr. Stokes: What level is proposed for FY 1993?

Dr. Shulman: In FY 1993, the NIAMS is estimating the funding level to be $10,541,000.

OSTEOPOROSIS

Mr. Stokes: The budget document states that osteoporosis is a major public health problem in the United States. It affects over 25 million Americans, mainly women 4 to 1. This is one of the few diseases where African American women are affected less often than white women. What type of research is being supported in this area?

Dr. Shulman: Although hip fractures are more common in white women than black women, the risk of hip fracture in black women over 75 is still considerable at one percent per year. A case-control study of the risk factors for hip fractures in black women and white women is underway that includes 30 hospitals in New York and Philadelphia. A major objective of the study is to identify whether there are different or similar risk factors for hip fracture in black women in comparison to white women.

Two studies of the black/white differences in bone structure and development were recently funded as a result of the FY 1991 NIAMS Initiatives in Osteoporosis. A study conducted at the Helen Hayes Hospital, Columbia University, and the Mount Sinai Medical Center in New York will explore the basic differences in bone structure, mass and turnover between blacks and whites. While blacks appear to have a higher bone mass at maturity and are less prone to vertebral and hip fractures, the reasons for these differences are not known.

Another study, funded as a result of the 1991 Request For Applications in Osteoporosis, is being conducted at Henry Ford Hospital in Detroit, and will focus on the accumulation and maximization of bone mass during the growth and development of children. Some of the goals of this investigation will be to relate bone mass and changes in bone mass to a variety of lifestyle factors, including diet patterns of exercise, as well as to determine the relationship of children's bone mass based on pre-pubertal bone mass and lifestyle, body size and familial factors. Male and female, Black, White, and Middle Eastern children will be included in the study.

An ongoing study at the Kaiser Foundation Research Institute is studying the potential determinants of bone density in a biracial population of over 700 male and female, Black and White, young adults, age 25-35. The major goal will be to determine what factors account for race and sex differences in skeletal metabolism at the time that peak bone mass is achieved. Since bone mass in early adulthood is believed to account for race and sex differences in the risk of osteoporotic fracture late in life, this study would increase knowledge of factors that may influence the future development of osteoporosis.

Washington area indicated that between 1960 and 1986 the incidence of squamous cell carcinoma increased 2.6 times in men and 3.1 times in women. Studies from Minnesota have indicated that between 1963 and 1978 the incidence of squamous cell carcinoma increased 2.5 times in men and 2.4 times in women.

Mr. Stokes: Do you have data available which indicates where we are compared to five years ago?

Dr. Shulman: In January of this year, the Centers for Disease Control published some data indicating that the melanoma death rates have continued to rise through 1988. However, several years are required before final data is available from large epidemiologic programs such as SEER.

Mr. Stokes: What factors are contributing to the increased incidence of skin cancer?

Dr. Shulman: Although there is evidence implicating a wide variety of factors in the etiology of skin cancer, the preponderance of scientific opinion is that the dramatic increases in the incidence of melanoma, squamous and basal-cell skin cancers are due to increased exposure to ultraviolet light. This increased exposure is thought to be a result of personal behavior-sunbathing or use of tanning lamps. It is feared that further increases in ultraviolet radiation exposure as a result of depletion of the stratospheric ozone layer may worsen the problem.

MINORITY EFFORTS

Mr. Stokes: How many and what percentage of employees of your institute are minorities?

Dr. Shulman: Overall, there are twenty-six minority individuals employed at the National Institute of Arthritis and Musculoskeletal and Skin Diseases. Out of a total of 114 permanent positions institute-wide, this represents 24 percent.

Mr. Stokes: Please provide a breakdown by race and grade level.

Dr. Shulman: A breakdown of minority employees of NIAMS, by race and grade, is as follows:

National Institute of Arthritis and Musculoskeletal and Skin Diseases
Minority Employees
FY 1991

	Blacks	Asians	Native Americans	Disabled
Grades 1-4	3			
Grades 5-8	10	2		
Grades 9-12	2	3	1	1
Grades 13-15	1	3		
TOTALS	16	8	1	14
PERCENTAGE	15%	7%	1%	1%

Mr. Stokes: How many are employed in a research capacity?

Dr. Shulman: Three minority individuals are employed in the Intramural Research Program and two in the Extramural Research Program.

Mr. Stokes: Please describe for the committee the resources and funding levels which will be provided for minority-specific research activities in FY 1993?

Dr. Shulman: The funding level for minority health research for FY 1993 is estimated to be $14,780,000.

Mr. Stokes: How do these levels compare to last year's levels?

Dr. Shulman: In FY 1992, the NIAMS estimates the spending level will be $14,025,000.

Mr. Stokes: Total funding represents what percentage of your budget?

Dr. Shulman: Minority Health research represents 7 percent of the NIAMS budget for both FY 1992 and FY 1993.

RHEUMATOID ARTHRITIS

Mr. Early: Will there be a specific research focus for the two new skin disease core centers?

Dr. Shulman: The guidelines for the Skin Diseases Research Cores Centers request that each applicant describe research themes they plan to develop further through the application. There is no specific research focus requested by NIAMS.

Mr. Early: I understand that NIAMS - supported researchers have found a new technological approach that should help in understanding rheumatoid arthritis. What can you tell us about this?

Dr. Shulman: Researchers have found many new technological approaches to help understand rheumatoid arthritis. Some of the new developments are:

- Small molecules that help cells communicate with one another behave abnormally in the joints of patients with rheumatoid arthritis. These molecules activate or inhibit the enzymes that destroy joints, help cells link together in inflammation, and control inflammation. Researchers believe that innovative modifications of these small molecules will lead to new treatments to control the disease.

- The precise genetic components of the disease are being uncovered. In some cases the molecules that identify the susceptibility gene are similar to molecules that are found in certain infectious agents. This may indicate how the immune system can be mobilized and then begin to attack a person's own joint tissues.

- Some parts of inflammation appear to be controlled very centrally in the brain. Animals that develop arthritis have a particular regulatory deficit in this area of the brain. This is a new approach to understanding how arthritis develops.

Mr. Early: In general, Doctor, what would you say are the two or three most promising areas of research on rheumatic diseases?

Dr. Shulman: One area is the very clear linkage of a specific genetic marker, HLA B27, with specific types of spinal arthritis. Workers have been able to create a transgenic rat with the human gene that reproduces the human disease in an animal model. This provides exceptional opportunities for research on understanding of how the disease develops and testing new treatment.

Another very promising area is understanding the ways in which inflammatory cells talk to one another. These cell activities are very finely tuned. A new era of biologics for treatment is being developed to control inflammation by manipulating the molecules by which cells communicate.

A third promising area is in the construction of more effective surgical prostheses, in which detailed understanding of the interaction of the implant and the surrounding tissue is leading to much more effective and long-lasting replacements for damaged joints.

EPIDERMOLYSIS BULLOSA

Mr. Early: It sounds as though the Institute has made a major advance in the area of Epidermolysis Bullosa. What progress can we look forward to next?

Dr. Shulman: Yes, sir, you are correct. The Institute has made major advances in the area of epidermolysis bullosa, a family of blistering diseases. Specific defects in two separate genes have been shown to cause two forms of EB, EB simplex and dominant dystrophic EB. As I discussed earlier, EB simplex causes superficial blistering of the skin's outer layer, the epidermis. The dominant dystrophic form of EB causes deeper blistering in the skin's inner layer, the dermis. Two groups of investigators discovered that EB simplex is caused by defects in genes for keratins. Another research team discovered that dominant dystrophic EB is linked with the gene for type VII collagen, a protein that helps attach the epidermis to the dermis.

EB simplex and dominant dystrophic EB, are disfiguring and functionally limiting, but they are not usually fatal. It is expected that in the near future, use of the same advanced molecular genetic technology will unveil the specific gene defects in lethal forms of EB that cause severe scarring. These include recessive dystrophic EB and junctional EB. With these defects known, investigators can learn the specific mechanism by which blistering takes place in these forms; and researchers can then fashion more directed therapeutic interventions. In addition, knowledge of the gene defects will allow physicians to make more precise diagnosis, aid genetic counseling for families with EB, and help researchers select appropriate patients for clinical trials. In these trials, the disease could be ameliorated or even reversed by suppressing the function of the normal gene or providing copies of the normal, undamaged gene.

The recent past history and near term future research in epidermolysis bullosa provides a compelling story of the productive application of cutting edge science to the understanding of the genetic disease. This work has been facilitated by cooperation between voluntary health agencies, researchers, and the NIH. Together they put into place--in the form of the EB registry--the facilities by which the breakthroughs could be made. They have now set the stage for therapeutic interventions at all levels, from classical treatment studies all the way to the potential for correcting of the basic underlying genetic defect.

Mr. Early: What are the Institute's plans for research on EB in FY 92 and FY 93?

Dr. Shulman: In FY 1992 and FY 1993, the NIAMS intends to continue the registry with expanded objectives that will allow for biostatistical and epidemiological evaluations of the data, as well as banking of a large number of tissue specimens to facilitate future research on EB. We have also issued a Program Announcement on the Biology of the Basement Membrane Zone of Skin and EB to encourage research in normal and diseased states with particular reference to epidermolysis bullosa.

Mr. Early: How much has been allocated for EB research in FY 92 and FY 93?

Dr. Shulman: The NIAMS has allocated $2,484,000 for EB research in FY 1992 and $3,708,000 in FY 1993.

OSTEOPOROSIS

Mr. Early: What progress can you report in osteoporosis research since you were here last year, Doctor?

Dr. Shulman: There has been a surge of new research on osteoporosis following the special initiatives in 1991. The response to the Requests for Applications (RFA) in osteoporosis was particularly gratifying. More than 120 applications were submitted and a large proportion of these were highly meritorious. We were able to fund 19 of the most outstanding proposals. Many of the applications not funded in FY 1991 are being revised and resubmitted and so this solicitation continues to fertilize the field of osteoporosis research.

One of the important aspects of providing special funds for a field such as osteoporosis is that scientists in related basic and clinical disciplines are encouraged to apply their knowledge to this particular disease. Three of the epidemiology projects that were awarded funds following the RFAs will make use of ongoing cohorts of subjects being studied in other fields but expand the area scrutinized to include osteoporosis. This will help benefit to increase our knowledge of the risk factors and possible preventive strategies for osteoporosis at a reasonable increase in cost to the overall project. Other investigators receiving funds as a result of these initiatives were newcomers to the field of osteoporosis.

The study of Osteoporotic Fractures-SOF, the largest multicenter epidemiologic project focused on the risk factors for falls and fractures competed for renewal this year. The peer review indicated that this project has been remarkably successful with the study of over 9,000 women over 65 years of age. This group has shown that in addition to hip, spine, and wrist fractures, previously known to be associated with low bone mass, that other low trauma fractures in women of this age can be predicted by knowledge of initial bone mass. The type of fracture can be predicted by knowledge of initial bone mass, also by the walking speed of the particular woman. Women who are frail and walk slowly tend to fall over sideways on the hip, thus sustaining the most serious type of fracture. Women walking more briskly will fall forward using their hand and arm to break their fall, and therefore, be at greater risk of wrist and forearm fractures.

This year there has been exciting research reported on a genetic mutation associated with a specific form of osteoporosis. Reports have previously suggested a familial predisposition to osteoporosis. A small subset of women with osteoporosis may have genetic abnormalities in type I collagen of the kind that are associated with the serious inherited bone disease of childhood, osteogenesis imperfecta. It is not clear at this time how many individuals classified as having osteoporosis are affected by these gene mutations. Other investigations of the genetic aspects of osteoporosis are focusing on regulatory molecules, such as vitamin D and osteocalcin, that promote bone accumulation.

Mr. Early: Would you tell us a little about the Women's Health initiative intervention and observational study in osteoporosis?

Dr. Shulman: The Women's Health Initiative proposed by Dr. Healy will be implemented this year with a contract awarded for a coordinating center. The planning process for this large and important study has involved the staff of many institutes, centers and divisions of the NIH. NIAMS staff have played a leadership role, particularly in the development of the osteoporosis component of the study.

The goal of this project is to focus on the major causes of death and disability in postmenopausal women; cancer, heart disease, and osteoporosis. There will be three different but integrated approaches to these problems. The first is an observational study of older women, (probably the largest study of this type ever conducted), to determine the risk factors and predictors of diseases in women including dietary, lifestyle, and medical and family history factors.

Concurrently, a major clinical trial, involving up to 60,000 women, will test the efficacy of a variety of interventions in preventing disease. The effect of postmenopausal hormone treatment on cardiovascular disease and osteoporotic fractures will be determined in conjunction with very close monitoring of adverse effects.

The second intervention study will be the effect of a low fat diet on the rate of breast cancer and heart disease. Women are tremendously concerned about the high rate of breast cancer in our country. One in nine American women will develop breast cancer in their lifetime. This is very much higher than in other countries such as Japan. While there may be genetic differences, diet also appears to be involved in the different rates of breast cancer cross-culturally.

The third intervention to be tested is supplementation with calcium and vitamin D on the rate of osteoporotic fractures and colon cancer. Previous studies and animal experimentation has indicated that high calcium diets may reduce both the rate of bone fractures and colon cancer.

In addition to the observational studies and the randomized intervention trial, the Women's Health Initiative will have a Community Intervention Component which will test the best ways to influence changes in health behavior in the community setting. These studies will compare paired communities where one community will receive information and incentive to change behaviors such as smoking, exercise, and fat consumption. The outcomes of this investigation will tell us how to best influence good health practices in the overall population.

Mr. Early: Would you tell us a little about the World Health Organization project on osteoporosis?

Dr. Shulman: The World Health Organization Cross-National Project on Osteoporosis will be a multinational study with cross-sectional, case-control, and longitudinal components. It is designed to ascertain and validate the incidence of hip fractures; to determine the age at which peak bone mass is attained; and to assess the loss of bone in different populations in the participating countries. The countries will be selected to represent a wide diversity of racial and ethnic populations including at least one country from Africa, Asia, South America and/or the Caribbean, and Europe, that are representative of minority and majority populations in the U.S.

The project will have five components and will be implemented in a step-wise fashion:

- The cross-national annual incidence of fracture of the hip in the population over 50 years of age will be assessed from hospital discharge data and from other sources of health information.

- A population survey will be undertaken to validate the hip fracture data available from these sources, with the goal of providing comparable prevalence and incidence rates from one country to another.

- A case-control study will be used to compare cross-cultural risk factors for fracture of the hip, such as family history, dietary habits, physical activity, medication use, sensory impairments, and smoking habits.

- A study of peak bone mass will assess the age of peak bone mass in each country, using Dual Energy X-ray Absorptiometry (DEXA), the factors affecting the peak bone mass, and the bone mass distribution in each age group after peak bone mass.

- A longitudinal study is planned in two age groups:

  a) The bone mass loss will be measured at 4 years follow-up in a group of individuals at the age of peak bone mass.

  b) Women in perimenopause and early menopause (50-59 years old) will be followed for 5 years to study the association between the occurrence of hip fracture and bone loss, calcium intake, physical activity, and gender.

Mr. Early: I understand that the Institute has enhanced its osteoporosis prevention and health promotion program. What actions have you taken?

Dr. Shulman: The NIAMS plans to award a contract for the establishment of a National Resource Center on Osteoporosis and Related Bone Disorders. The resource center will focus on osteoporosis, as well as Paget's disease of bone, osteogenesis imperfecta, and other bone disorders. The Resource Center will work closely with public and private organizations to disseminate information about these disorders and serve as a catalyst for the development of prevention and education approaches. Audiences served will include the public, patients, and their families, and health professionals.

As an early step on gathering information for the Resource Center, NIAMS has recently produced an "Osteoporosis Prevention and Education: A Research Guide" for patients, the general public, and health professionals. This guide identifies specific organizations and programs that offer education, training, screening, and other services specific to osteoporosis. The guide also provides an annotated bibliography of lay and professional material and should be available for distribution by April 1992.

WOMEN'S HEALTH INITIATIVE

Mr. Early: Doctor, your institute has responsibility for research on a number of diseases and disabilities which disproportionately affect women. Would you have highlight some of the initiatives planned under the Women's Health initiative in these other areas?

Dr. Shulman: There are two new and exciting foci for research on women's health at the NIH-the Women's Health Initiative-WHI and the Office of Research on Women's Health-ORWH. We have outlined above for you the objectives, activities, and phases of the Women's Health Initiative.

The planning process for the Women's Health Initiative involved the staff of many of the institutes, centers, and divisions of the NIH and NIAMS in a leadership role, particularly in the osteoporosis component of the study. The goal of this project is to focus on the major causes of death and disability in postmenopausal women; cancer, heart disease, and osteoporosis. There will be three different but integrated approaches to these problems. The first is an observational study of older women, to determine the risk factors and predictors of diseases in women including dietary, lifestyle, and medical and family history factors. Concurrently, a major clinical trial, involving up to 60,000 women, will test the efficacy of a variety of interventions in preventing disease.

The second intervention studied will be the effect of a low fat dietary pattern on the rate of breast cancer and heart disease. While there may be genetic differences, diet also appears to be involved in the different rates of breast cancer cross-culturally. If a lower fat diet can be shown to reduce the rate of this devastating disease, there will be a great incentive for women to change their dietary habits.

The third intervention to be tested is supplementation with calcium and vitamin D on the rate of osteoporotic fractures and colon cancer. Smaller studies and animal experimentation has indicated that high calcium diets may reduce both the rate of bone fractures and colon cancer cases.

The Women's Health Initiative will have a Community Intervention Component that will test the best ways to influence changes in health behavior in the community setting. These studies will compare paired communities where one community will receive information and incentive to change behaviors such as smoking, exercise, and fat consumption. The outcomes of this investigation will tell us how to best influence good health practices in the overall population.

In addition to these very specific and focused activities of the Women's Health Initiative, opportunities for enhanced activities that focus on women's health and the particular disease of women are being facilitated by the new Office of Research on Women's Health. This office plays a role in coordinating and encouraging the activities throughout NIH in the area of women's health. In September of 1991, the ORWH held a very successful meeting to develop a research agenda on women's health. Dr. Pinn, Director of ORWH, is now implementing that research agenda by offering to support research supplements and to cofund projects in collaboration with the funding components of the NIH. The projects selected for supplementation or co-funding will be those given the highest priority in the recently developed research agenda. NIAMS has a major interest and a high level of activity in the disease that affect women disproportionately and we expect to collaborate extensively with the ORWH.

Several important areas of NIAMS research--osteoporosis, lupus, rheumatoid arthritis, and others--are important components of the overall research agenda of the Office of Research on Women's Health (ORWH). NIAMS expects that several of the upcoming initiatives will be jointly sponsored by ORWH and NIAMS.

CLINICAL RESEARCH

Mr. Early: Doctor, in your opening statement, you mention a new endeavor to pursue opportunities for clinical investigations and clinical trials in a number of areas. Would you highlight a few of these for us, and then expand on this for the record?

Dr. Shulman: In four separate workshops, we convened experts in arthritis, skin disease, bone disease, and musculoskeletal disorders to discuss the need for clinical studies in these areas. Each workshop has identified specific studies that should be addressed over the next ten years.
Examples of major clinical trials in the arthritis program include Methotrexate in the Treatment of Systemic Lupus Erythematosus, Treatment of Erythema Migrans,and Early and Aggressive Combination Therapies for Rheumatoid Arthritis. Examples of major clinical trials in the skin diseases program include Treatment of Chronic Wounds and Gamma Interferon For Treating Atopic Dermatitis. Examples of major clinical trials in the bone diseases include Long Term Effects of Exercise and Diet on Peak Bone Mass, Assessment of Combinations of Preventive Interventions for Postmenopausal Osteoporosis, and Biosphsphonates for Treatment of Bone Disease. Examples of major clinical trials in the musculoskeletal program include Cemented versus Cementless Total Hip Replacements and Treatment of Spinal Stenosis.

Mr. Early: Does your budget request allow you to implement any of these clinical investigations and trials to any significant degree?

Dr. Shulman: The FY 1993 Budget funds our highest priorities. As you know, in science, our opportunities for clinical investigation and trials far outstrip our resources. Therefore, it is our challenge to fund only the very best proposals.

SPORTS MEDICINE

Mr. Early: Your Institute also supports research on sports injury and repetitive motion syndrome. What sort of collaboration is there between your institute and CDC's injury control program an NIOSH?

Dr. Shulman: NIAMS cosponsored with NIOSH a Workshop on National Strategy for Occupational Musculoskeletal Injuries: Implementation Efforts and Research Needs. NIAMS staff presented a paper and chaired a session at that workshop. NIAMS has participated in the review of the draft document for further research. Preliminary discussions have been held with NIOSH and leaders of the research field regarding means to stimulate more research. A Workshop on Sports Injuries in Youth: Surveillance Strategies was sponsored by NIAMS and our National Advisory Board. Collaborators from the CDC participated in the steering committee to plan the workshop and presented papers during the meeting.

BIOMATERIALS

Mr. Early: Tell us something about NIAMS research program on biomaterials.

Dr. Shulman: NIAMS supports research on orthopaedic biomaterials with a special emphasis on those utilized in total joint replacement. Investigators consider not only the biomaterials and their surface properties, but also the body's response as a host to these implanted devices. One research area involves the attachment of porous-coated prosthetic devices to the host by ingrowth of the bone into the device surface. Another area of study concerns the release of wear products-especially from high density polyethylene-which may produce foreign body reactions and weakening of the supporting bone structure.

Mr. Early: Is your Institute playing a role in the advanced materials and processing program?

Dr. Shulman: NIAMS staff participated in committee meetings to generate the NIH response in support of the Advanced Materials and Processing Program. Detailed information was provided on both the categorization of current activities supported by NIAMS and our potential role in enhanced activities in the future.

Mr. Early: What can you tell us about the programs of excellence in Orthopaedic Biomaterials?

Dr. Shulman: Program(s) of Excellence in Orthopaedic Biomaterials is a proposed research grant activity under the Advanced Materials and Processing Program. The objective is to fund a critical mass of scientific investigators to lead the US towards continuing its worldwide leadership in the development of new generation orthopaedic devices. These programs would focus on mechanisms of interrelationships between the biomaterial implant and inflammation, infection, wound healing, repair, growth, and degradation. The ultimate goal of this coordinated effort would be fundamental understanding that would lead to more effective long-term orthopaedic implants and improve the quality of life of the recipient.

Mr. Early: How much are you allocating for your biomaterials research program in FY 92 and FY 93?

Dr. Shulman: The NIAMS is allocating $7,498,000 for biomaterials research program in FY 1992 and $8,000,000 in FY 1993.

Mr. Early: Is there any new money?

Dr. Shulman: There is an approximately $500,000 increase available for biomaterials research.

Mr. Early: Last year, you indicated that your Institute expected to have a close working relationship with the new National Center for Medical Rehabilitation Research. Do you have any collaborative efforts planned for FY 92 and 93?

Dr. Shulman: In addition to a large grant portfolio devoted to and relevant for rehabilitation research, the NIAMS participates as an ex officio member of the Advisory Board of the National Center for Rehabilitation Research. The NIAMS is also collaborating on a conference on Prosthetics and Orthotics and a conference on Osteogenesis Imperfecta, both with the National Center for Rehabilitation Research.

RESEARCH PROJECT GRANTS

Mr. Early: What is the projected "success rate" for your Institute and how does this compare to FY 92 and FY 91?

Dr. Shulman: The projected "success rate" for FY 1993 is 22.1 percent, compared to 23.5 percent in FY 1992 and 31.3 percent in FY 1991.

Mr. Early: To what payline percentile will the Institute be able to fund under the budget request and how does this compare to FY 92 and FY 91?

Dr. Shulman: In FY 1993, our estimated payline percentile will be 20.0 percent. For FY 1992 the payline percentile is estimated to be 21.0 and for FY 1991 it was 29.6 percent.

Mr. Early: What is the average increase in the size of noncompeting research project grants under the budget proposal?

Dr. Shulman: The average increase in the size of noncompeting research project grants is 3.4 percent.

Mr. Early: What about new and competing research grants?

Dr. Shulman: The average increase for new and competing grants is 4.9 percent.

Mr. Early: What was the downward adjustment for noncompeting grants in FY 91 and FY 92?

Dr. Shulman: The downward adjustment rate is no longer being used. All noncompeting grants will receive a four percent cost-of-living increment.

Mr. Early: What are you projecting for FY 93?

Dr. Shulman: The same policy of a four percent increase will continue in FY 1993.

Mr. Early: Will the NIAMS be able to fund noncompeting grants at the commitment level under the FY 93 request?

Dr. Shulman: NIH now has a policy of indexing out-year commitments to four percent over the prior year. Using these commitment levels as benchmarks, downward adjustments on noncompeting grants will no longer occur.

Mr. Early: Will the NIAMS be able to fund new and competing grants at the peer reviewed levels?

Dr. Shulman: Competing research project grants will continue to be reviewed by the scientific staff of the Institute, and appropriate budget adjustments will be made.

CLINICAL TRIALS

Mr. Early: Are there any clinical trials that could be undertaken in FY 93 if additional resources were available?

Dr. Shulman: There are 16 new clinical trials that could be initiated in FY 1993 with additional funding and personnel.

Mr. Early: Would you give us some examples of those approved but unfunded trials which you consider to be a high priority and tell us why?

Dr. Shulman: Examples of clinical trials and clinical investigations of high priority to NIAMS include:

- Biologic agents as treatments for rheumatic diseases
- Aggressive combination therapies for rheumatoid arthritis
- Methotrexate in the treatment of lupus
- Treatment of anti-phospholipid syndromes
- Effects of exercise and diet on peak bone mass
- Biophosphonates for treatment of bone diseases

- Treatment of anterior knee pain
- Treatment of chronic wounds
- Gamma interferon for treating atopic dermatitis

New and imaginative clinical trials mechanisms need to be developed to address these important disease areas.

Mr. Early: Please provide for the record a list of approved but unfunded clinical trials, along with a brief description of the trial, its duration, the first year cost and the estimated total cost of the trial.

Dr. Shulman: The following is a list of approved but unfunded clinical trials in the FY 1993 request:

National Institute of Arthritis and Musculoskeletal and Skin Diseases
Major New Clinical Trial Initiatives
FY 1993: Unfunded within the President's Request
(Dollars in thousands)

	First Year Cost	Total Cost	Duration (Years)
Biologic Agents as Treatments for Rheumatic Diseases:			
Extramural (EP)	600	3,900	5
Intramural (IRP)	500	3,500	5
Early and Aggressive Combination Therapies for Rheumatoid Arthritis:	700	10,500	8
Treatment for Erythema Migrans (Early Lyme Disease):	1,000	3,500	3
Treatment of Late Lyme Disease:	600	1,750	3
Treatment of Anterior Knee Pain:	800	3,500	3
Methotrexate in the Treatment of Systemic Lupus Erythematosus:	800	2,500	3
Treatment of Anti-Phospholipid Syndromes:	700	3,000	4
Long-term Effects of Exercise and Diet on Peak Bone Mass:	1,000	7,500	10
Assessment of Combinations of Preventive Interventions for Postmenopausal Osteoporosis:	1,000	17,500	8

Biosphosphonates for Treatment of Bone Diseases:	1,000	3,000	3
Cemented versus Cementless Total Hip Replacements:	1,000	10,000	8
Treatment of Spinal Stenosis:	500	2,500	3
Efficacy of 13-cis Retonic Acid and Other Derivatives in the Treatment of Keratinizing Disorders:	1,000	3,500	3
Treatment of Chronic Wounds	1,000	5,500	4
Gamma Interferon for Treating Atopic Dermatitis:	500	2,500	4
TOTALS	12,700	84,150	

RESEARCH CENTERS

Mr. Early: What was the level of downward adjustment in the centers program in FY 91 and FY 92?

Dr. Shulman: Across-the-board adjustments are no longer used. For FY 1991, FY 1992, and FY 1993, budget adjustments will be made on competing centers individually.

Mr. Early: What is the estimate for FY 93?

Dr. Shulman: Budget adjustments for competing centers will be made on an individual basis in FY 1993. NIH now has a policy of indexing out-year commitments to four percent over the previous year using commitment levels as benchmarks.

Mr. Early: Doctor, will the NIAMS be able to fund noncompeting centers at commitment levels under the budget request?

Dr. Shulman: Requests for adjustments will be made on an individual basis.

Mr. Early: Will the NIAMS be able to fund competing centers at the peer reviewed levels?

Dr. Shulman: Competing center grants will continue to be reviewed by the scientific staff of the Institute, and appropriate adjustments will be made on an individual basis.

Mr. Early: How do you plan to support the same number of centers in FY 93 and FY 92 with no increase in funds?

Dr. Shulman: All centers will be reviewed on an individual basis and budget adjustments will be made as necessary.

FINANCIAL MANAGEMENT PLAN

Mr. Early: Is NIAMS plan making greater use of "out of order" funding to achieve a lower cost per award?

Dr. Shulman: The NIAMS does not plan to make any greater use of the out of order funding to achieve a lower cost per award. We use the "out of order" funding to stimulate areas of research that need more attention and also to explore innovative ideas. Decisions to fund out of order are made on both a programmatic and scientific basis.

Mr. Early: Is limiting the average increase in the cost per award having an impact on your Institute's research programs, particularly with respect to clinical research and clinical trials?

Dr. Shulman: As with all research project grants, we will be carefully reviewing each individually to ensure that any budget adjustments are not deleterious to the science proposed in the project. Many of our large clinical trials are conducted using the research and development contract mechanism. During the negotiation process, the costs for the trial's scope and duration are determined.

PROFESSIONAL JUDGMENT BUDGET

Mr. Early: What was the NIAMS Professional Judgment Budget and how does it differ from the request before us?

Dr. Shulman: The NIAMS Professional Judgment Budget was $301,313,000. This would increase the number of investigator initiated competing research project grants from 184 to 423, a difference of 239 competing grants. The number of centers would increase by 8, from 28 to 36 including two additional skin diseases research centers and six specialized centers of research. The number of research career awards would increase by 29 and data project and demonstration projects would increase by three. Research trainees would increase by 68 from 228 to 296 and clinical trials would increase by four, from 19 to 35. Our Intramural Research program would develop a Connective Tissue Research Laboratory and the Orthopaedic Research Laboratory, and our Research Management and Support program would increase to support the additional staff necessary to provide the scientific leadership and overall management direction of the entire Institute.

Mr. Early: Will any significant new research initiatives or opportunities be lost or delayed by lack of funds in the FY 93 budget request?

Dr. Shulman: The Institute has numerous meritorious research projects in all diseases within its mandate that will be delayed. Listed below are some of the research opportunities that could be pursued if funds were available, however, the Institute will fund its highest priority within the FY 1993 budget request.

- Lupus: Research to explain the predominance of lupus in women, especially black women.
- Rheumatoid arthritis: Aggressive treatment of early established rheumatoid arthritis.
- Lyme disease: Enhanced research in Lyme disease and its treatment.
- Osteoarthritis: Treatment and rehabilitation in osteoarthritis.
- Bone diseases and bone biology -- including osteoporosis and Paget's disease.
- Estrogen: Mechanism of action of estrogen on bone.
- Low back pain: Multidisciplinary research on low back pain.
- Sports medicine: Exercise, musculoskeletal fitness and sports medicine.
- Heritable diseases: Basic connective tissue research for hereditary diseases.
- Psoriasis: Molecular genetic basis of psoriasis.
- Wound healing: Molecular events in wound healing.
- Bullous diseases: Molecular basis of autoimmune bullous diseases.
- Rehabilitation: Mechanisms of skeletal muscle degeneration and development of regenerative and training interventions to maximally rehabilitate muscle function.
- Skin diseases: Skin diseases, such as vitiligo, alopecia, and epidermolysis bullosa.
- Ultraviolet radiation: Basic research on keratins and the molecular basis of skin sensitivity to ultraviolet radiation.

Mr. Early: What priorities would the Institute pursue if additional resources were available?

Dr. Shulman: In FY 1991 the Institute funded 228 new and competing grants. This number dropped to 194 in the current fiscal year. Our first priority would be to restore the number of new and competing awards to the FY 1992 level and, if possible, to exceed that level. I believe we need to fund at least one out of every three approved grant applications if we are going to maintain a vigorous biomedical research enterprise in arthritis and musculoskeletal and skin diseases research.

Another high priority is the expansion of our centers program, for example, additional specialized centers of research (SCORs) in certain diseases, lupus, and arthritis in children, and two more skin research centers. At present, NIAMS has SCORs only in osteoporosis, osteoarthritis, and rheumatoid arthritis.

Research training and career development is another high priority area. Three years ago, the Institute's National Advisory Board carried out an analysis of NIAMS training and career development needs. The three at the top of the list are the (a) establishment of research training opportunities in epidemiology/clinical trials, (b) creation of mechanisms similar to minority supplements for physically handicapped individuals, and (c) expansion of the Institute's career development (K series) programs. The last is especially important because the K series awards enable physicians with clinical training in diseases under the mandate of NIAMS to develop and/or update skills in related laboratory-based research.

Scientists in the Institute's intramural program on connective tissue research wish to develop a connective tissue research laboratory. These tissues, which are subject to attack and injury by arthritis and musculoskeletal and skin diseases, are found in almost all parts of the body, binding together and providing support for various organs and structures. Establishment of a Laboratory of Connective Tissue Biology was a main component of the plan submitted to Congress in 1988, and it represents the Institute's number one priority for the next major, intramural expansion.

Mr. Early: If an increase over the FY 93 request is provided, how would you use these additional funds?

Dr. Shulman: As you know, Mr. Early, NIAMS has spent the last year or so finalizing the NIAMS National Plan. This document, in fact, inventories the progress and advances that have been made in the areas of research supported by the NIAMS and outlines future research directions. The plan has enabled us to identify more clearly the research needs and opportunities that hold promise for discovering the causes, new treatments and prevention of many of the disabling, long-term diseases, affecting the millions of Americans, for which this Institute has responsibility. The plan identifies promising areas of research for the several hundred diseases within the mandate of the NIAMS, and the Institute will use the National Plan in conjunction with the NIH Strategic Framework to guide us in addressing these research needs over the next 5 to 10 years. Given the breadth and depth of our programs and research needs it is difficult to summarize our priorities; however, our highest priorities are as follows:

- Expand our portfolio of clinical investigations and clinical trials in rheumatic diseases, musculoskeletal diseases, bone diseases, muscle diseases, and skin diseases.

- Expand our knowledge of genetic predisposition to diseases within the research mandate of NIAMS.

- Introduce biologics and molecular control of diseases.

- Expand our knowledge of the source of race and sex distribution of diseases.

HERITABLE DISORDERS OF CONNECTIVE TISSUE

Mr. Mrazek: What is your best judgement of the number of heritable connective tissue disorders?

Dr. Shulman: Heritable disorders of connective tissues refer to conditions in which genetically based defects lead directly or indirectly to structurally weak or abnormal matrix proteins in connective tissues. Participants at the Workshop on Heritable Disorders of Connective Tissue, cosponsored by NIAMS in April 1990, estimated that there are approximately 200 distinct heritable disorders of connective tissue. Osteogenesis imperfecta, Ehlers-Danlos syndrome, Marfan's syndrome, epidermolysis bullosa, cutis laxa, and the chondrodysplasias are some of the more familiar of these disorders.

Osteogenesis imperfecta is a heterogeneous group of disorders of bone fragility. The most significant feature of this genetic disorder is the susceptibility of affected infants and children to bone fractures from very mild trauma. Ehlers-Danlos syndrome is a group of about a dozen disorders characterized by soft and hyperextensible skin and joint laxity. Marfan's syndrome is characterized by aortic aneurysms and dissection, long limbs and tall stature, marked joint hypermobility, flexion contractures, scoliosis, and lens dislocation. Epidermolysis bullosa is a group of inherited skin diseases in which defects in the attachment of the outer layers of skin result in blistering and scarring. Cutis laxa is a disorder with marked looseness of the skin which may be accompanied by internal organ abnormalities. The chondrodysplasias are inherited disorders of linear bone growth. More than 150 forms of these disorders have been identified.

Mr. Mrazek: How many people in the United States are affected?

Dr. Shulman: According to scientists participating in the April 1990 Workshop, there are nearly half a million people affected with heritable disorders of connective tissue in the United States. It is also possible that many more individuals have milder forms of these disorders.

Mr. Mrazek: What is the status of research on heritable disorders of connective tissue?

Dr. Shulman: Research is progressing rapidly in identifying biochemical and genetic defects in connective tissue of individuals with heritable disorders. For example, in Marfan Syndrome, the protein fibrillin has been shown to the defective and unable to produce strong elastic tissues. Genetic linkage studies have determined that the defect gene is located on chromosome 15. There are a wide array of clinical expressions arising from the genetic defects in many of these diseases. Investigators believe that many common medical conditions, such as osteoarthritis and osteoporosis, may represent expression of mild mutations in some cases. Future research would focus on more detailed understanding of the specific relationships between genetic mutations and the functional manifestations.

Mr. Mrazek: For which disorders have genes been identified?

Dr. Shulman: There are over 200 distinct heritable disorders of connective tissue. All of these have a mutation(s) in genes that encode for matrix proteins or in genes ultimately affect the structures of the extracellular matrix. In many of the disorders-such as, osteogenesis imperfecta, epidermolysis bullosa, Ehlers-Danlos syndromes, Marfan Syndrome, pseudoxanthoma elasticum, and chondrodysplasias-a specific defect has been identified for one or more of the clinical forms of the disease. With improved technology for molecular biologic research it is likely that genetic defects can be uncovered for most conditions.

Mr. Mrazek: Can you assess the impact of the 1990 NIAMS Conference on Heritable Disorders of Connective Tissue?

Dr. Shulman: The chairpersons of the Conference prepared a summary article that includes sections on the state-of-knowledge and future directions of research in heritable disorders of connective tissue. This article was recently accepted for publication in the scientific journal Matrix. NIAMS program staff also prepared a brief layperson summary, which was given to the Foundation for Heritable Disorders of Connective Tissue. NIAMS has prepared a Program Announcement, in cooperation with the National Institute of Child Health and Human Development (NICHD) encouraging additional research that will be released in the NIH Guide for Grants and Contracts by mid-April. This announcement specifically refers to the research recommendations generated during the Conference.

Mr. Mrazek: Has it generated significant scientific interest in these diseases?

Dr. Shulman: It is difficult to measure the full impact until the Program Announcement has been received by investigators and time has permitted the generation of research applications. At a recent research society meeting, investigators discussed with NIAMS program staff collaborative clinical studies that may be considered as a means of combining patient populations to enhance research productivity. Therefore, there appears to be a high level of scientific interest.

Mr. Mrazek: Is NIAMS considering issuing a program announcement to support continued molecular research on heritable disorders of connective tissue?

Dr. Shulman: NIAMS and the National Institute of Child Health and Human Development (NICHD) plan to issue a program announcement that will be published in the NIH guide in the next two to three weeks to encourage research to investigate specific molecular defects of hereditary diseases of connective tissue.

Mr. Mrazek: Is NIAMS considering the development of a national registry to facilitate research on heritable connective tissue diseases?

Dr. Shulman: NIAMS will continue to consider possible options for the establishment of registries in the area of heritable diseases of connective tissue. Registries are valuable but tend to be quite expensive and current resources will not allow for the support of new registries containing a research support component. NIAMS is considering suggesting the initiation of rosters of patients as a less expensive alternative.

NIH STRATEGIC PLAN

Mr. Pursell: Where does the NIAMS fit into the NIH strategic plan?

Dr. Shulman: The NIAMS has a vital interest in the NIH Strategic Plan. The scope of the research effort quite naturally generates a number of complex issues, demanding a logical and comprehensive action plan for the responsible distribution of scarce public resources. Through the integration of both the NIH and the NIAMS plans, improving and safeguarding the health of every man, woman, and child in this country is closer to attainment.

NIAMS staff has taken an active role in developing the framework for the NIH Strategic Plan. The scientific community's input serves an invaluable function, as the NIAMS National Advisory Board and its National Advisory Council have discussed many of these concerns extensively.

The fourteen panels convened to address the issues of the NIAMS National Plan are directly related in so many different ways to those targeted by the objectives and plans contained in the NIH framework. Much of the research in the disease areas primary to the NIAMS mission fit under the headings of critical technologies; such as, molecular medicine, biotechnology, and structural biology. Several other important areas of NIAMS research address the second NIH planning objective of enhancing research capacity in fields such as chronic and recurrent illness and rehabilitation, aging, health of women and minorities, prevention, childhood health, and population-based studies. Mutual progress toward the expansion of the nation's research capacity and intellectual capital will provide the means necessary for achievement in the research enterprise for health.

OUTREACH PROGRAMS

Mr. Pursell: What outreach programs are the institute undertaking to be more responsive to the community?

Dr. Shulman: Several outreach programs have been developed by our Multipurpose Arthritis and Musculoskeletal Diseases Centers.

Here are two examples of education programs for patients with arthritis that are helping patients deal with arthritis and to lead more active lives. One program is the Arthritis Self-Management Program developed by Dr. Lorig and Dr. Holman of Stanford University. This is a six week standardized course that can be conducted by lay leaders. The course covers information about arthritis, training in exercise and relaxation programs, joint protection methods, nutrition practices, decision-making about non-traditional remedies, physician-patient communications, and techniques for solving arthritis-related problems. A long-term study of patients who have completed this course demonstrated that they have less pain and are more active than patients who have not taken the course. This course is now offered throughout the United States through the Arthritis Foundation and is being adopted in Australia and Canada. The other is the EDUCIZE program that was developed by Ms. Connell at Northwestern University. This course combines aerobic exercise with problem-solving discussions in a community hospital for elderly persons with rheumatoid arthritis.

Within the Institute, the Office of Scientific and Health Communications (OSHC) is the focus of outreach and community-education related activities. An important emphasis is the dissemination of new research findings to the public through the media, voluntary and professional organizations, and other audiences. These means include conferences, news releases and news stories on important findings, annual research reports on arthritis and related disorders and in other areas such as genetics and aging, and invitations to media to cover NIAMS conferences and workshops, along with publications, by NIAMS program staff, of conference proceedings.

To answer the thousands of public requests for information we receive each year, this office has created information packages, fact sheets, resource lists and other materials that enable the distribution to be responsive to specific and general requests. We have at least 40 different information packages--listing other information sources and containing several carefully screened recent articles--on commonly requested subjects.

NIAMS also has some special ongoing education and information efforts:

- A major one is the National Arthritis and Musculoskeletal and Skin Diseases Information Clearinghouse. The Clearinghouse serves as a national resource center for information about professional, patient, and public education materials; community demonstration programs; and Federal programs related to rheumatic, musculoskeletal and skin diseases. Functions of the Clearinghouse include maintaining a database of these materials that is a subfile of CHID (the Combined Health Information Database), responding to inquiries, and developing extensive bibliographies on education materials. This year a major bibliography has been created on scleroderma, working with key experts and voluntary groups in this field.

- Another important effort is the Task Force on Lupus in High Risk Populations. The purpose of the Task Force is to develop educational strategies directed to patients, the public and health professionals that may help improve the outcome of lupus in populations at increased risk for lupus. We have sent some 2,000 kits to community organizations to help them develop programs; and 30,000 copies of our brochure "What Black Women Should Know About Lupus" have beendistributed in the first six months of the campaign.

- The Institute has also implemented several projects on Lyme disease education and information in collaboration with the National Institute of Allergy and Infectious Diseases. These include distribution of conference results on diagnosis and treatment; continued production of "Lyme Lines: Lyme Disease Research News From NIH" for professional audiences; creation of a prevention poster; and development of a public brochure.
- The NIAMS has placed much greater emphasis on information and education activities in osteoporosis. This year we have created "Osteoporosis Prevention and Education: A Resource Guide" for health professionals and health educators, identifying about 130 national and local programs and hundreds of published materials. Most importantly, we are about to competitively advertise for contract proposals to run a National Resource Center on Osteoporosis and Related Bone Disorders. The Center will coordinate and collaborate with public and private organizations to respond to information requests and serve as a catalyst for education programs on osteoporosis, Paget's disease, osteogenesis imperfecta and related bone disorders. Audiences will include the public, patients, and health professionals.

Mr. Pursell: What clinical programs are there for the community based rheumatologist?

Dr. Shulman: Community rheumatologists now participate in NIAMS-funded activities, such as treatment trials funded through a group of cooperative clinics in a national data base funded by the NIAMS. Greater involvement of community-based rheumatologists in other clinical trials is under active consideration.

SKIN DISEASE RESEARCH

Mr. Pursell: Dr. Shulman, I met with a number of patient advocates for increased funding for skin disease research. They were all excited with advances recently being made in the field and also indicated that your institute works very closely with them. Could you give us a feeling for how the whole field of skin disease research is coming along, and what kind of strategies you have laid out for research in this area?

Dr. Shulman: Skin Disease research has been making rapid advances on many fronts. Utilizing current state-of-the-art techniques of molecular biology and molecular genetics, scientists are greatly enhancing our understanding of various cutaneous diseases. Among the most exciting recent discoveries are the identification of the genes underlying two forms of epidermolysis bullosa, the delineation of the molecular basis of pemphigus, pinpointing of genetic defects of albinism, evidence of inflammatory processes involved in psoriasis, and greater insight into the role of ultraviolet light in the development of melanoma and nonmelanoma skin cancer.

The Institute is fostering additional research on skin diseases through a variety of mechanisms. In the past year, NIAMS has issued program announcements on: the Molecular and Structural Biology of Hair and its Diseases With Special Reference to Alopecia Areata; Cutaneous Manifestations of HIV Infection and AIDS; Biology of the Basement Membrane Zone of Skin and Epidermolysis Bullosa; and the Etiopathogenesis and Treatment of Psoriasis.

In addition, the Institute works closely with voluntary health agencies in coordinating support of research in skin diseases. For instance, we are referencing the tissue bank that will soon be established by the National Psoriasis Foundation, and we continue to collaborate with Dystrophic Epidermolysis Bullosa Research Association (DEBRA) to recruit patients for the National Epidermolysis Bullosa Registry. The EB Registry is now undergoing recompetition for an additional five years of funding.

As a result of the growing scientific opportunities and interest expressed by the research community, as well as the success of the two currently operating skin disease centers, NIAMS issued a request for applications (RFA) in November 1991 for additional centers. The Institute intends to fund two more Skin Disease Core Centers in FY 1992 in response to this RFA. Future plans also include a workshop on wound healing, an area of great medical interest and of major impact health care costs in the United States.

Mr. Pursell: Is my understanding correct that you held a large planning conference to develop such a strategy?

Dr. Shulman: In February of 1991, the NIAMS held a large planning meeting to create a National Research Plan for the Institute. This document includes a comprehensive section on skin diseases. The document is in its final stages of preparation and will be available shortly.

Mr. Pursell: Also, tell us about skin cancer and especially malignant melanoma -- did you have a consensus conference on that recently?

Dr. Shulman: The Consensus Development Conference panel made a number of recommendations. In the area of prevention, they suggested avoidance of excessive exposure to ultraviolet radiation, especially in those with a family history of greater than normal susceptibility to melanoma. With regard to diagnosis, the panel advocated discontinuing use of the controversial term "dysplastic nevus syndrome" and developing less confusing histological criteria. New studies were cited showing that when doctors remove tiny areas of healthy skin around the least-advanced lesions, patients are just as likely to survive as when more skin is removed. This led the panel to conclude that surgical treatment should be limited to conservative margins.

JUVENILE ARTHRITIS

Mr. Young: Dr. Shulman, can you summarize the Institute's research program in the area of Pediatric Arthritis?

Dr. Shulman: In the area of juvenile arthritis, NIAMS-supported investigators are engaged in research on the genetic factors, the human leukocyte antigen (HLA) genes, in the various forms of arthritis in children. Using new techniques in molecular biology, they are finding that the genetic markers are distinct for different types of arthritis in children. In addition, NIAMS-supported researchers at one of our multipurpose arthritis and musculoskeletal centers are conducting basic research on the causes of juvenile dermatomyositis, a serious disease causing muscle pain and weakness.

Much work remains to be accomplished in expanding our understanding of the causes of arthritis in children, and more researchers need to be trained to specialize in this field. NIAMS plans to encourage more research grant applications in this very important area.

Mr. Young: How much funding has been spent on Pediatric Arthritis research to date?

Dr. Shulman: NIAMS estimates $663 thousand of its 1992 appropriation specifically for juvenile arthritis. However, overall our Institute is spending $107.6 million of its total $203.9 million appropriation for research on arthritis and related diseases. Many of the conclusions drawn from arthritis research in adults relate directly to juvenile arthritis.

Mr. Young: Dr. Shulman, what are your future plans for supporting research in Pediatric Rheumatology, particularly systemic lupus, osteoporosis, and juvenile rheumatoid arthritis?

Dr. Shulman: The NIAMS actively encourages research in all forms of arthritis and other rheumatic diseases affecting children. It has specific initiatives requesting additional research in Lyme disease that affects so many children and juvenile arthritis. The NIAMS also supports research in systemic lupus erythematosus and dermatomyositis in children. Osteoporosis in children is usually related to chronic illness and/or its treatment. NIAMS grantees are studying different ways of treatment that will protect the bones of children with arthritis and with systemic lupus.

Mr. Young: Dr. Shulman, there are a limited number of researchers in Pediatric Rheumatology, as it is a new field. What are your plans to improve and increase research in this area?

Dr. Shulman: The NIAMS supports a research fellow, through its intramural program, in pediatric rheumatology and encourages the inclusion of pediatricians in its training and fellowship funding mechanisms. Similarly, the NIAMS encourages the applications for research training and career development awards in pediatric rheumatology.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

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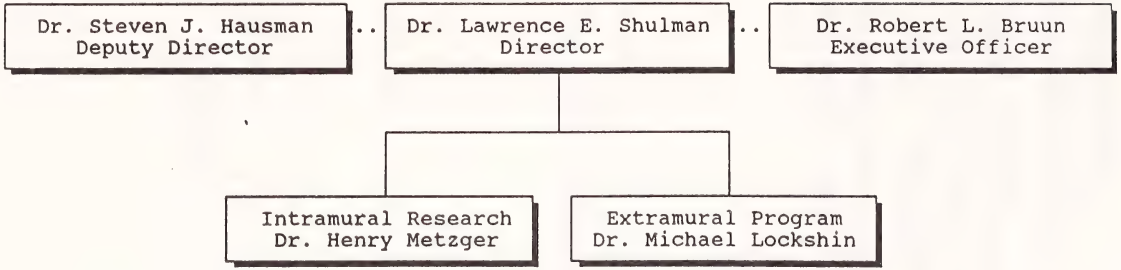
NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Organization Structure



NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

For carrying out section 301 and title IV of the Public Health Service Act with respect to arthritis and musculoskeletal and skin diseases, [$204,502,000] *$214,929,000*: *Provided*, That of the funds made available under this heading, [$7,593,000] *$9,318,000* shall not become available for obligation until September 30, [1992] *1993*.

(Departments of Labor, Health and Human Services, and Education and Related Agencies Appropriation Act, 1992.)

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Amounts Available for Obligation 1/

	1991 Actual	1992 Appropriation	1993 Estimate
Appropriation	$198,442,000	$204,502,000	$214,929,000
Sequester Order	-3,000	---	---
Section 514(a) reduction	-412,000	---	---
Section 514(b) reduction	-4,783,000	---	---
Section 214 travel reduction	---	-45,000	---
Section 513(a) travel reduction	---	-73,000	---
Section 513(a) S & E reduction	---	-971,000	---
Subtotal, adjusted appropriation	193,244,000	203,413,000	214,929,000
Real transfer from: NCI for cancer research	---	500,000	---
Real transfer from/to: Other accounts for Shannon Awards	222,000	---	---
Subtotal, adjusted budget authority	193,466,000	203,913,000	214,929,000
Unobligated balance lapsing	-17,000	---	---
Total obligations	193,449,000	203,913,000	214,929,000

1/ Excludes the following amounts for reimbursable activities carried out under this account: FY 1991 -- $2,729,000; FY 1992 -- $2,490,000; FY 1993 -- $2,600,000.

NATIONAL INS UTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Budget Mechanism

(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	No.	Amount	No.	Amount	No.	Amount
Research projects:						
Noncompeting.............	482	$90,263	529	$100,625	562	$110,538
Administrative supplemental...........	(28)	1,063	(17)	627	(17)	650
Competing:						
Renewal................	78	17,027	76	17,303	72	19,477
New....................	149	24,009	116	19,546	110	17,191
Supplemental...........	1	50	2	106	2	110
Subtotal, competing..	228	41,086	194	36,955	184	36,778
Subtotal, research projects	710	132,412	723	138,207	746	147,966
Research centers:						
Specialized/ Comprehensive centers..	26	20,660	28	22,961	28	22,961
Other Research:						
Research career programs.	59	4,387	58	4,421	58	4,421
Minority biomedical research support.......		400		420		420
Other research related...	55	2,685	22	1,884	22	1,884
Subtotal, other research...	114	7,472	80	6,725	80	6,725
Total, research grants.....	850	160,544	831	167,893	854	177,652

Training						
Individual awards						
Noncompeting	19	540	24	692	21	609
Competing:						
Renewal	0	0	0	0	0	0
New	16	486	11	351	14	434
Subtotal, individual	35	1,026	35	1,043	35	1,043
Institutional awards						
Noncompeting	140	4,028	166	4,996	167	5,104
Competing:						
Renewal	32	1,022	20	583	22	601
New	8	298	7	232	4	106
Subtotal, institutional	180	5,348	193	5,811	193	5,811
Total, training	215	6,374	228	6,854	228	6,854
Research and development contracts	16	2,977	19	4,018	19	4,018
	FTE		FTE		FTE	
Intramural research	69	14,491	72	15,753	75	16,550
Research management and support	69	9,080	69	9,395	71	9,855
TOTAL BUDGET AUTHORITY	138	193,466	141	203,913	146	214,929
Clinical Trials		(6,717)		(7,502)		(7,803)

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

CROSSWALK - 1991 Actual

(Dollars in thousands)

MECHANISM

PROGRAM ACTIVITY	Research Grants			Training Programs		Research and Development Contracts	Intramural Research	Research Management and Support	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional				
Arthritis, Musculoskeletal and Skin Diseases......	$132,412	$20,660	$7,472	$1,026	$5,348	$2,977			$169,895
Intramural Research.							$14,491		14,491
Research Management and Support........								$9,080	9,080
Total Budget Authority	132,412	20,660	7,472	1,026	5,348	2,977	14,491	9,080	193,466

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

CROSSWALK - 1992 Appropriation

(Dollars in thousands)

MECHANISM

PROGRAM ACTIVITY	Research Grants			Training Programs		Research and Development Contracts	Intramural Research	Research Management and Support	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional				
Arthritis, Musculoskeletal and Skin Diseases......	$138,207	$22,961	$6,725	$1,043	$5,811	$4,018			$178,765
Intramural Research.							$15,753		15,753
Research Management and Support.......								$9,395	9,395
Total Budget Authority	138,207	22,961	6,725	1,043	5,811	4,018	15,753	9,395	203,913

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

CROSSWALK - 1993 Estimate

(Dollars in thousands)

MECHANISM

PROGRAM ACTIVITY	Research Grants			Training Programs		Research and Development Contracts	Intramural Research	Research Management and Support	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional				
Arthritis, Musculoskeletal and Skin Diseases......	$147,966	$22,961	$6,725	$1,043	$5,811	$4,018			$188,524
Intramural Research.							$16,550		16,550
Research Management and Support.......								$9,855	9,855
Total Budget Authority	147,966	22,961	6,725	1,043	5,811	4,018	16,550	9,855	214,929

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Summary of Changes

1992 Estimated budget authority..........................	$203,913,000
1993 Estimated budget authority..........................	214,929,000
Net Change..	+11,016,000

	1992 Current Estimate Base		Change from Base	
Changes:	Pos. (FTEs)	Budget Authority	Pos. (FTEs)	Budget Authority
A. **Built-in:**				
1. FY 1993 pay raise		$9,046,000		+$249,000
2. Annualization of 1992 pay increases.................		9 046,000		+95,000
3. Within grade increases..........		9,046,000		+98,000
4. One day less pay................		9,046,000		-35,000
5. Payment for centrally furnished services............		8,686,000		+621,000
6. Increased cost of laboratory supplies, materials, and other expenses................		7,416,000		+113,000
7. Service and supply fund increase		1,048,000		+188,000
8. DHHS Working Capital Fund.......		219,000		+11,000
Subtotal...................				+1,340,000
B. **Program:**	No.	Amount	No.	Amount
1. Research projects:				
a. Noncompeting..............	529	101,252,000	+33	+9,936,000
b. Competing.................	194	36,955,000	-10	-177,000
Subtotal..................	723	138,207,000	+23	+9,759,000
	Pos. (FTEs)		Pos. (FTEs)	
2. Intramural Research.............	72	15,753,000	+3	---
3. Intramural Research: program decrease.....................	72	15,753,000		-56,000
4. Research Management and Support......................	69	9,395,000	+2	---
5. Research Management and Support: program decrease....	69	9,395,000		-27,000
Subtotal.................			+5	+9,676,000
Total changes............			+5	+11,016,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Budget Authority by Activity

(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	FTEs	Amount	FTEs	Amount	FTEs	Amount
Arthritis and musculoskeletal and skin diseases........		$169,895		$178,765		$188,524
Intramural research....	69	14,474	72	15,753	75	16,550
Research management and support..........	69	9,080	69	9,395	71	9,855
Subtotal, obligations	138	193,449	141	203,913	146	214,929
Unobligated balance lapsing.............		17		---		---
Total, Budget Authority	138	193,466	141	203,913	146	214,929
HIV/AIDS	(4)	(1,633)	(4)	(1,727)	(4)	(1,813)

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Budget Authority by Object

	1992 Appropriation	1993 Estimate	Increase or Decrease
Full-time equivalent of permanent positions	117	122	+5
Total compensable workyears:			
Full-time equivalent employment	143	148	+5
Full-time equivalent of overtime and holiday hours	2	2	---
Average ES salary	$103,366	$107,191	+3,825
Average GM/GS grade	9.6	9.6	---
Average GM/GS salary	36,578	37,931	+1,353
Average salary, grades est. by act of July 1, 1944 (42 USC 207)	82,757	85,819	+3,062
Average salary of ungraded positions	---	---	---
Personnel Compensation:			
Full-time permanent	$4,700,000	$4,972,000	+$272,000
Other than full-time permanent	1,515,000	1,666,000	+151,000
Other personnel compensation	345,000	323,000	-22,000
Special personnel services	807,000	738,000	-69,000
Subtotal, personnel compensation	7,367,000	7,699,000	+332,000
Personnel benefits	1,679,000	1,754,000	+75,000
Benefits for former personnel	0	0	0
Travel and transportation of persons	173,000	248,000	+75,000
Transportation of things	46,000	69,000	+23,000

	1992 Appropriation	1993 Estimate	Increase or Decrease
Rent, communications and utilities...	$228,000	$248,000	+$20,000
Printing and reproduction............	126,000	106,000	-20,000
Other Services:			
Project contracts..................	4,018,000	4,018,000	0
Centrally furnished services.......	8,686,000	9,307,000	+621,000
Standard level user charge.........	0	0	0
Other..............................	3,063,000	3,052,000	-11,000
Supplies and materials..............	2,180,000	1,863,000	-317,000
Equipment...........................	1,600,000	2,059,000	+459,000
Grants, subsidies and contributions..	174,747,000	184,506,000	+9,759,000
TOTAL......................	203,913,000	214,929,000	+11,016,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Significant Items in the House and Senate Appropriations Committee Reports

Lupus

The House in its report 102-121, page 91, stated "...The Committee directs the NIAMS to establish an SLE project team. This team should develop a strategic plan for coordinating SLE research and identifying benchmark standards by which to assess progress in this field. The Committee has provided additional funds over the President's budget for this project."

The Senate in its report 102-104, page 130, stated "The Committee continues to be very supportive of investigation in the area of Lupus and urges that priority be given to this area."

Action Taken or To Be Taken - NIAMS has assembled a lupus research team whose purposes are to assess current knowledge on lupus and to develop plans for future research. As a major stimulus to these efforts, the Institute organized an important innovative "Scientific Workshop: A Future Research Agenda for SLE," held January 1992. The workshop involved an in-depth discussion on the causes of lupus including immunologic mechanisms, genetic factors, and environmental factors. Questions such as why is SLE predominantly a women's disease, why is SLE predominantly in young women, why is SLE more common in blacks, and new approaches to treatment were also addressed. Based on the recommendations from the workshop, the Institute plans to issue several program announcements.

NIAMS continues to place, as it has in the past, a high priority on lupus research. In September 1991, NIAMS, in collaboration with the National Heart, Lung, and Blood Institute, sponsored a workshop entitled "Antiphospholipid Antibody/Lupus Anticoagulant Workshop." Approximately one-third of lupus patients have an antibody (antiphospholipid or lupus anticoagulant) that is associated with early failure of the placenta, which in turn can cause the patient to have a miscarriage. The workshop identified research recommendations that have resulted in the planned issuance of a program announcement by NIAMS and NHLBI to encourage submission of grant applications specifically relevant to antiphospholipid antibody and lupus anticoagulant.

In January 1992, the Institute held a meeting to further its collaborative efforts on SLE with leaders of the scientific community in the Caribbean. The goals of the workshop were to establish in-depth dialogue between Caribbean and U.S investigators interested in epidemiologic studies of lupus in Caribbean populations, to generate specific pilot research proposals, to identify next steps for further collaboration, and to identify training needs and resources. This population will provide a unique opportunity to investigate both genetic and environmental factors that determine why lupus is more common in black than white women. Following the workshop the Institute plans to issue a program announcement for collaborative epidemiologic studies of SLE in Caribbean populations targeted at understanding racial differences in SLE.

NIAMS has had tremendous success with its outreach and education efforts with the activities of its Lupus Task Force. A brochure entitled "What Black Women Should Know About Lupus" has been distributed to national organizations for health, community groups, churches, libraries, health care facilities, schools, and other community organizations. As of December 1991, over 23,000 copies of the brochure had been distributed and requests for materials continue to come in. Future lupus education plans include an enhanced outreach effort targeted toward health professionals.

Osteoporosis

The House in its report 102-121, page 91, stated "The Committee encourages the National Institute on Arthritis and Musculoskeletal and Skin Diseases to continue to expand and intensify programs of research, education, and health promotion aimed at reducing the prevalence of osteoporosis."

"...Missing is a central point for providing scientifically accurate and up-to-date information on osteoporosis. The Committee recognizes the need for a resource center and urges its establishment outside of NIH in order to assure the range of issues it addresses exceeds those normally permitted by NIH."

The Senate in its reports 102-104, page 128 stated "The Committee would like to ensure that those who have osteoporosis, their families, and those concerned about the disease have a means of obtaining the most up-to-date, scientifically accurate information. The Committee encourages...[NIH] to establish a resource center which can provide information and materials and coordinate education for physicians and allied health professional. Additionally, the center should include a resource library, a means for tracking activities at the State level, and a range of information on services for those with osteoporosis."

Action Taken or To Be Taken - NIAMS leads the DHHS effort to conduct and support basic, clinical, and epidemiologic studies on the causes, diagnosis, treatment, and prevention of osteoporosis and osteoporosis-related fractures. In the past year, NIAMS has intensified its efforts in this area. Within the extramural program, the Institute has elevated the Bone Biology and Bone Diseases Program to the status of a Branch.

In February 1991, NIAMS issued two requests for applications (RFAs), one for basic research on osteoporosis, and a second on clinical and epidemiologic research on osteoporosis. The response from the research community was exceptional (123 grant applications); NIAMS awarded 19 new grants in the fall of 1991, 11 in the area of basic research and 8 for clinical and epidemiologic research.

In addition, NIAMS issued an RFA to invite grant applications from interested institutions for Specialized Centers of Research (SCORs) in three areas of special interest to the Institute, including osteoporosis. This represents the first recompetition of the NIAMS SCOR program, begun in 1987.

NIAMS expects to award funding for nine SCORs, three each in osteoporosis, osteoarthritis, and rheumatoid arthritis.

NIAMS has also enhanced its osteoporosis prevention and health promotion activities. The NIAMS will award in the Fall 1992 a contract for the establishment of the Resource Center on Osteoporosis and Related Bone Disorders. The center will facilitate and enhance knowledge and understanding of osteoporosis and related bone disorders by disseminating information on research findings, services, and educational materials to patients, health professionals, and the public. Similarly, in early 1992, NIAMS will distribute an Osteoporosis Prevention and Education Resource Guide, prepared by the Institute for patients, the general public, and health professionals. The guide will identify specific organizations and programs that offer education, training, referrals, screening, and other services specific to osteoporosis.

In recognition of the growing scientific knowledge about the causes and treatments of osteoporosis, the Institute planned a number of workshops and conferences to further facilitate the dissemination of information. In December 1991, the Institute sponsored an international meeting on biochemical markers for bone turnover. Other meetings planned for fiscal year 1992 include an a workshop on Clinical Investigations/Trials in Bone Diseases; a workshop on Osteoporosis and Oral Bone Loss (with NIDR); and a workshop on research directions for osteoporosis.

The Senate in its report 102-104, page 150, stated "...The committee directs the NIH, in coordination with the Agency for Health Care Policy and Research, to conduct research related to identifying and evaluating cost-effectiveness strategies for prevention, diagnosis, and treatment of osteoporosis and related bone disorders."

"...Further, the Committee requests that a report be given to the Committee prior to the fiscal year 1993 hearings breaking out efforts to date by various institutes and future plans for initiatives."

Action Taken or To Be Taken - NIAMS, in collaboration with the Agency for Health Care Policy and Research (AHCPR), is planning to organize and cosponsor a workshop to examine Research Needs on Cost-Effective Strategies on Osteoporosis and Other Bone Disorders. The workshop will focus on reviewing the current state of knowledge on cost-effectiveness research in osteoporosis, identifying research opportunities, considering collaborative roles for NIH and AHCPR in future activities, and setting an agenda for future research efforts.

A report describing research, related activities, and future plans of four NIH institutes and the AHCPR regarding cost-effectiveness strategies for osteoporosis and other bone disorders has been prepared for the Committee. The report was prepared by NIAMS in collaboration with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Institute on Aging (NIA), the National Institute of Dental Research (NIDR), and AHCPR.

Lyme Disease

The Senate in its report 102-104, page 129, stated "...The Committee urges continued high priority be placed on Lyme disease."

Action Taken or To Be Taken - NIAMS continues to place high priority on research directed at increasing knowledge of the causes, treatments, and preventive strategies for Lyme disease. As a result of an RFA issued in April 1991, the Institute has funded nine new grants for research on the diagnosis and treatment of the disease.

In addition, NIAMS has been highly active in generating collaborative efforts with the research community, in concert with the National Institute of Allergy and Infectious Diseases (NIAID), in pursuing research on Lyme disease. In September 1991, NIAMS and NIAID hosted the second annual meeting of 14 grantees who were funded through an April 1989 RFA. This type of forum, which brings grantees together annually to discuss their ongoing research, has proven to be highly successful. It is an effective means of coordinating research efforts in this area.

The Institute, in collaboration with NIAID, sponsored a state-of-the-art workshop on the Diagnosis and Treatment of Lyme Disease in the spring of 1991. The report of the proceedings has been published and distributed to 65,000 primary care physicians and health professionals.

Public information and education efforts on Lyme disease continue with the distribution of Lyme Lines, a semiannual newsletter on Lyme disease, published jointly by NIAMS and NIAID. The newsletter is routinely distributed to NIAMS and NIAID grantees, relevant voluntary and professional organizations, and State health departments.

Scleroderma

The House in its report 102-121, page 93, stated "...The Committee strongly urges the Institute to increase its research on the causes of scleroderma, to gain new insight into the relationship between the blood vessel pathology and the connective tissue overgrowth that occurs in scleroderma, and to continue to explain the role of the immune system."

Action Taken or To Be Taken - On October 28-29, 1991, NIAMS and the National Advisory Board for Arthritis and Musculoskeletal and Skin Diseases sponsored a scientific workshop on the Biology and Pathology of Acquired Connective Tissue Diseases. A major component of the workshop was devoted to scleroderma. National experts in scleroderma research discussed major advances and identified future research directions.

A second workshop specifically devoted to research on scleroderma (systemic scleroses) and other related fibrotic disorders is planned for fiscal year 1992. The workshop will be followed by a program announcement seeking additional research proposals in this field.

A bibliography of research literature on scleroderma has been developed for health professionals, including nurses and medical librarians.

Osteogenesis Imperfecta

The Senate in its report 102-104, page 131, stated "...The Committee would like to see continued emphasis on this brittle bone disease."

"...The Committee is very concerned that at present there is no postpediatric care for individuals with osteogenesis imperfecta. The

Committee would like to see NIAMS support the training of medical professionals in the field."

Action Taken or To Be Taken - NIAMS has given and continues to give high priority to research in the area of osteogenesis imperfecta. As part of its increased emphasis on bone biology and bone diseases, the Institute has a growing portfolio of investigator-initiated research it is supporting in the area of brittle bone disease. In addition, the Institute plans to support a fellowship for a research investigator who plans to train in the genetic analysis of collagen, a research area extremely relevant to osteogenesis imperfecta.

Heritable Disorders of Connective Tissue

The House in its report 102-121, page 93, stated "...The Committee remains concerned about these patients and their families and encourages continued work on these problems."

The Senate in its report 102-104, page 131, stated "...The Committee urges NIAMS to follow up on the 1990 workshop findings by issuing a program announcement to support continued molecular research on identifying the chromosomal marker and gene component of these individual disorders that can then be transferred into improved therapies and treatments. NIAMS is also urged to consider and develop plans for a national registry to facilitate research on these heritable connective tissue diseases."

Action Taken or To Be Taken - The Institute has developed plans for an initiative that will investigate the specific molecular defect(s) of the hereditary diseaes of connective tissue (those not caused by spontaneous mutations) and mechanisms by which these alterations result in disease. Several diseases, including osteogenesis imperfecta, Ehlers-Danlos syndrome, muscular dystrophy, have specific molecular defects that have been identified. The mechanisms by which these defects result in disease, however, remains to be elucidated; opportunities abound for similar studies in other connective tissue disorders.

Paget's Disease

The Senate in its report 102-104,page 130, stated "...The Committee is pleased that the NIAMS has taken the lead among the NIH institutes in targeting research on Paget's disease bone disorders. The Committee requests NIAMS to provide an NIH-wide report on its plans to address this particular disease entity."

Action Taken or To Be Taken - An NIH-wide report has been prepared under the auspices of the Arthritis and Musculoskeletal Diseases Interagency Coordinating Committee (AMDICC). The report provides an overview of the research activities of seven NIH institutes and centers in the area of Paget's disease and related bone disorders.

Skin Disease

The Senate in its report 102-104, page 131, stated "...The Committee urges the Institute to establish two additional skin disease research centers, as the two currently existing skin disease centers have proven the value of this kind of organization."

Action Taken or To Be Taken - As a result of the growing scientific opportunities and interest expressed by the research community as well as the success of the two currently operating skin disease centers, NIAMS issued an RFA in November 1991 for additional centers. The Institute intends to fund two additional Skin Disease Core Centers in FY 1992 in response to this RFA.

Alopecia Areata

The House in its report 102-121, page 93, stated "...The Committee requests NIAMS to report back to the Committee no later than January 31, 1992, on research that is being funded by the Institute on alopecia areata and what research is planned over the next several years."

Action Taken or To Be Taken - A report has been prepared for the Committee that summarizes current and future NIAMS-supported research activities in the area of alopecia areata. NIAMS continues to be interested in furthering research to expand knowledge of the etiology and pathogenesis of alopecia areata. The proceedings of the October 1990 workshop, cosponsored by NIAMS and the Alopecia Areata Foundation, have been published as a supplement to the May 1991 issue of the Journal of Investigative Dermatology. In May 1991, NIAMS issued a PA to encourage submission of research and fellowship grant applications in the area of hair biology and disease with special reference to alopecia areata.

Neuroskeletal Diseases

The House in its report 102-121, page 94, stated "The Committee is fully supportive of research in the area of neuroskeletal diseases and encourages increased attention to these problems."

The Senate in its report 102-104, page 129, stated " The Committee urges consideration of the establishment of a neuroskeletal science center for the study of neurological and skeletal disorders."

Action Taken or To Be Taken - NIAMS supports a considerable amount of research on muscle and skeletal function and diseases of the musculoskeletal system. This research portfolio includes research in the area of muscle diseases, including the muscular dystrophies and myotonias; bone diseases; and exercise physiology, including neurological control and coordination of the musculoskeletal system. Of growing interest to the institute and the research community is the relationship between neurological function and dysfunction and the musculoskeletal system and the limitations in musculoskeletal function due to injury and pain. The Institute will continue to explore opportunities to support scientific research in this area.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1992 Amount Authorized	1992 Appropriation	1993 Amount Authorized	1993 Budget Request
Research and Investigation.........	Section 301	42 § 241	Indefinite	>$197,059,000	Indefinite	>$208,075,000
National Institute of Arthritis and Musculoskeletal and Skin Diseases..................	Title IV	42 § 285d, 1 thru 7	Indefinite		Indefinite	
National Research Service Awards...	Title IV Part F	42 § 288	Authorizing legislation pending. 1/	6,854,000	Authorizing legislation pending. 1/	6,854,000
Total Budget Authority........				203,913,000		214,929,000

1/ This training authority is shared with other research training programs of the National Institutes of Health and the Alcohol, Drug Abuse and Mental Health Administration.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Appropriation History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1987	$106,733,000	$140,225,000	$129,475,000	$138,713,000
1988	123,009,000	---	---	---
1988	132,089,000	154,632,000	153,867,000	147,679,000
1989	158,244,000 2/	155,487,000 2/	161,244,000 2/	159,897,000 3/
1990	167,334,000 4/	171,673,000	171,688,000	171,250,000 5/
1990 Sequester				-2,320,000
1991	176,080,000	191,397,000 6/	198,746,000	193,247,000 7/
1991 Sequester				-3,000
1992	204,797,000	204,977,000	203,076,000	203,413,000 8/
1993	214,929,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.

2/ Excludes funds for AIDS research and education ($687,000).

3/ Excludes funds for AIDS research and education ($673,000), for Gramm-Rudman-Hollings spending targets ($1,943,000), and for the FY 1989 Procurement Reform Reduction ($91,000).

4/ The 1990 request excludes funds for the National HIV program ($1,254,000) proposed for consolidation in the Office of the Assistant Secretary for Health.

5/ Excludes enacted administrative reductions of $431,000.

6/ Excludes funds for NRSA training, which is unauthorized.

7/ Excludes enacted administrative reductions of $5,195,000.

8/ Excludes enacted administrative reductions of $1,089,000.

Justification

National Institute of Arthritis and Musculoskeletal and Skin Diseases

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
138	$193,466,000	141	$203,913,000	146	$214,929,000	+5	+$11,016,000

General Statement

Since its inception in 1986, the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) has made great strides in investigating several of the rheumatic diseases, disorders of the musculoskeletal system, and diseases of the skin, and in improving knowledge of the normal structure and function of joints, muscles, bones, and skin. These diseases afflict millions of Americans causing tremendous human suffering and economic loss both to the individuals affected and to the Nation. Women, minorities, and the elderly are frequently and predominantly affected.

The NIAMS seeks to discover underlying disease mechanisms; reduce suffering; provide the means to control, cure, and ultimately, prevent disease; and to disseminate widely the results of research. To this end, the Institute conducts and supports basic research in a wide variety of scientific disciplines, including immunology, molecular biology, structural biology, genetics, biochemistry, physiology, virology, and pharmacology. The NIAMS also supports and conducts multifaceted clinical research in the fields of rheumatology, bone diseases, orthopaedics, sports medicine, and dermatology.

During the past year--NIAMS research has generated scientific advances that enhance knowledge about underlying disease mechanisms, treatment regimens, and ways to improve patient care.

Among the Institute's major concerns are the rheumatic diseases, which afflict more than 37 million Americans and cause an annual loss of billions of dollars to the Nation's economy. The Institute supports a variety of research efforts designed to reveal the pathology of these disorders and offer therapeutic measures to the patient. Rheumatic diseases cover over 100 diseases including rheumatoid arthritis, scleroderma, systemic lupus erythematosus (SLE), infectious rheumatic diseases such as Lyme disease, and osteoarthritis. This is a research field of tremendous cross fertilization, where advances in one disease area often reveal research opportunities in others.

Over the last decade, scientists gained a clearer understanding of the genetics of rheumatoid arthritis, the mechanisms of joint destruction, and the control of the inflammatory process involved in this disease. These advances brought improvement in therapies, including new anti-inflammatory agents, with fewer side effects and new therapeutic agents, such as methotrexate, that interfere with basic mechanisms that induce arthritis. Progress also was made in assessing long-term patient outcomes, and in developing and using protheses to replace severely damaged joints.

NIAMS-supported investigators are exploring clinical research opportunities in the treatment of rheumatoid arthritis. In a major multicenter clinical trial, the drug minocycline is being used to treat rheumatoid arthritis. The objective of the study is to determine whether minocycline hydrochloride produces clinical improvement and to determine what side effects rheumatoid arthritis patients may experience from the minocycline therapy.

In other areas of treatment, NIAMS-supported researchers have recently explored the properties of a drug that appears to act differently from aspirin and other nonsteroidal antiinflammatory drugs (NSAIDs) in the destructive inflammation of rheumatoid arthritis. The drug, tenidap sodium, inhibits the inflammation triggered by a family of compounds called leukotrienes. Treatment of rheumatoid arthritis with new agents that go beyond action of aspirin and NSAIDS may alter the progressive joint damage so commonly seen in patients with rheumatoid arthritis.

This year, NIAMS supported researchers found an interesting new approach for treating rheumatoid arthritis. This procedure, called extracorporeal photochemotherapy is a process by which cells are removed from an rheumatoid arthritis patient, treated, and then reinfused back into the patient. In patients treated for 6 months, a positive clinical response was observed. Researchers found improvement in grip strength, walking time, and morning stiffness. This new technological approach greatly improves the understanding of the immune mechanisms that underlie rheumatoid arthritis in addition to improving an effective therapy.

Systemic lupus erythematosus (SLE), is a serious health problem that primarily effects young women. Over the past decade, researchers have clarified the immunogenetics of lupus, identified and separated new syndromes that have special treatment requirements such as subcutaneous lupus, and published the results of long-term treatment trials that have reoriented our thinking about the treatment of patients with major life threatening complications.

In 1991, the NIAMS implemented important initiatives designed to further the understanding of systemic lupus erythematosus (SLE) and educate those which it strikes. Incidence, prevalence, and mortality figures show that lupus strikes 9 times more women than men and 3 times more black women than white women. NIAMS recently initiated studies in different parts of the country on racial characteristics of black women to discover factors that may contribute to their increased risk of developing SLE. These studies should provide valuable information on the genetic aspects of affected women. A NIAMS-supported initiative to collect data on the genetic backgrounds of two separate populations in the Caribbean may also shed important genetic information on why certain minority populations are at increased risk for this disease. These are a few of the studies designed to shed light on how SLE develops and what ways it may be blocked or prevented.

The NIAMS began a targeted education campaign to educate young black women about the symptoms of SLE, its diagnosis and treatment. This campaign is generating media attention and helping to educate women about the disease nationally at the community level.

Scleroderma, another rheumatic disease that predominantly strikes women, is characterized by excessive accumulations of the structural protein collagen in the skin and loss of small blood vessels. It is a serious life threatening disease also affecting vital organs such as the heart, kidneys, lungs, and gastrointestinal tract. These deposits can cause thickening and hardening of the connective tissues, hence the term "scleroderma" or "hard skin."

This year, NIAMS-supported investigators made the exciting discovery that the activity of endothelin, a new protein substance produced by blood capillaries, is coupled with two important features of scleroderma--clamping (vasoconstriction) of small blood vessels, and the overproduction of collagen. Blood vessels of patients with scleroderma commonly constrict for long periods, thus destroying sensitive body parts. This finding, which connects two apparently unrelated symptoms of the disease, is intriguing. Further investigation of how this protein works offers a new opportunity to develop an effective treatment against this aggressive, life-threatening disease.

Lyme disease is an infectious illness caused by a small organism, the spirochete Borrelia burgdorferi. The spirochete is spread to humans by the deer tick, Ixodes dammini. Lyme disease, once contracted, may seriously affect the joints and skin, in addition to the nervous system and other parts of the body. Between 1982 and 1990, more than 30,000 cases of Lyme disease were diagnosed. Many areas of the country are heavily infested with Lyme disease, and this contagion has become the most common tick-borne illness in the United States. Yet it remains one of the most mysterious because its symptoms can vary tremendously, it eludes diagnosis by blood tests, and it persists in some individuals to cause chronic, painful joint arthritis.

To discuss the definition, diagnosis, and treatment of Lyme disease, NIAMS and NIAID convened a state-of-the-art workshop in the spring of 1991, in which clinicians and researchers discussed the problems they face in diagnosing and treating the disorder. In the fall of this past year, NIAMS and NIAID grantees met to discuss recent progress in basic research to understand the pathology of the disease, detect the spirochete, and to design effective treatments at the molecular level. Research findings made by NIAMS grantees have improved our understanding in many areas: why certain people stricken with Lyme disease are prone to develop chronic arthritis; what parts of the spirochete may be attacked chemically to render it inert; and which diagnostic tests are the most sensitive and specific in detecting infection. Results will soon be available from a NIAMS-supported regional study to determine whether giving antibiotics to individuals who suffer a tick bite reduces the incidence of Lyme disease.

Osteoarthritis, or degenerative joint disease, is the most common form of arthritis, affecting some 16 million Americans. This disease primarily affects cartilage, the protective material that covers and cushions the ends of the bones, causing it to fray, wear, ulcerate, and, in extreme cases disappear entirely, leaving a bone-on-bone joint.

Advances have been made in understanding the treatment of osteoarthritis. NIAMS investigators followed one animal model of joint instability for many years and proved, for the first time, that instability at the knee does lead to true osteoarthritis. Recent research conducted by investigators at one of the NIAMS-supported Specialized Centers of Research on Osteoarthritis has shown that acetaminophen (a pain-killer or analgesic) is as effective as ibuprofen (a nonsteroidal anti-inflammatory drug or NSAID), for symptomatic treatment of osteoarthritis of the knee. This study showed that there were no significant differences between acetaminophen and ibuprofen and that, in fact, acetaminophen, which is less costly and less toxic, may be a better treatment for osteoarthritis. The results from this study were duplicated by other NIAMS-supported investigators in a long term multicenter trial.

The Institute currently supports a broad spectrum of research in the area of musculoskeletal diseases. These diseases, which are leading causes of disability among people in all age groups, include such chronic diseases as osteoporosis, Paget's disease of bone, and inherited diseases such as Duchenne's muscular dystrophy, Marfan syndrome, and osteogenesis imperfecta.

In the past year, NIAMS has intensified its research efforts in the area of osteoporosis and related bone diseases. A recent request for research applications on osteoporosis has generated 123 responses in three months, resulting in the award of 19 new grants, 11 in the area of basic research and 8 with respect to clinical and epidemiologic research. NIAMS support for osteoporosis research includes, not only laboratory studies focusing on basic biology of the disease, but also epidemiologic and clinical research to discover risk factors associated with the disease.

An important research advance in understanding the molecular basis for osteoporosis was the recent duplication, or cloning, of the cell receptor for calcitonin. Calcitonin, a hormone released from thyroid, attaches to the receptor on osteoclasts, cells that break down bone, and inhibits their activity. The cloning of this new receptor adds insights into the control of osteoclast development and function, and thus may help researchers improve the control of bone loss associated with osteoporosis.

NIAMS-supported researchers are currently exploring further the interesting findings suggesting that older people can exercise safely and routinely to maintain bone density, yet still avoid injury. Exploration of activities that reduce bone loss in older individuals are extremely important in curbing the tremendous morbidity of the elderly due to frailty and fractures in limbs that are weakened by osteoporosis.

Duchenne muscular dystrophy (DMD) is a devastating muscle disease resulting from a defect in the gene that codes for a large membrane-associated protein called dystrophin. The severity of DMD is related to the nature and location of the defect on the dystrophin gene. Researchers recently synthesized a full-length replica of the dystrophin gene and inserted it into established cell cultures, resulting in synthesis of protein that is indistinguishable from naturally occurring dystrophin. This provides opportunities to determine the role of dystrophin in normal and diseased individuals; and could be the first step toward the initiation of gene therapy.

Marfan syndrome is one of the most common inherited connective tissue disorders. It is characterized by skeletal, ocular, and cardiovascular abnormalities. It is difficult to diagnose because of the extreme variability of clinical expression. Marfan syndrome has been found to be associated with fibrillin, a major connective tissue protein. In the summer of 1991, several teams of investigators reported the location of the gene for fibrillin on human chromosome 15. This discovery will aid greatly in the diagnosis of the disorder and lead eventually to therapy.

A transgenic mouse model has been developed that mimics a mild form of human osteogenesis imperfecta, a devastating connective tissue disorder characterized by bone fragility causing multiple fractures in early life. The model carries a mutation in a structural gene for type I collagen. This will enable researchers to study the effects of type I collagen on the structure and function of bone. It will also offer an experimental system in which to test therapies designed to strengthen both mineralized and nonmineralized connective tissue.

New knowledge about the structural foundation of skin is leading to new advances in the area of blistering skin diseases, wound healing, and the aging skin. Separate, creative research approaches by three teams of investigators have revealed why the skin disintegrates in a group of hereditary blistering diseases. These combined NIAMS-supported studies have unveiled the molecular bases of a set of rare but devastating diseases, epidermolysis bullosa (EB), for which specific therapies can now be pursued.

Psoriasis is a common, chronic inflammatory skin condition that affects many Americans, some so severely that they must be hospitalized. Plaque psoriasis is unsightly, debilitating, and often resistant to treatment. NIAMS-supported researchers this year published results of a clinical trial to compare doses of cyclosporine used to treat plaque psoriasis. The careful design of dosing regimens is important because cyclosporine is potentially very toxic. The study confirms that cyclosporine therapy leads to a rapid and thorough clearing of severe recalcitrant psoriasis. It also indicates that an initial low dose of 5 mg per kg per day is safe and effective in treating severe psoriasis.

NIAMS initiatives are diverse and vigorous. They range from basic biotechnological efforts, such as the production of the first transgenic animal with a key functional molecule of the human immune system that is directly responsible for a major form of arthritis to clinical trials in rheumatic, bone, and skin diseases.

Initiatives to expand the intramural program have led to basic research payoffs in understanding skin disease and structural biology at the macromolecular level. In addition, the intramural program offers unique training opportunities, such as fellowships in pediatric rheumatology and biomechanics.

Women and minorities, who are affected by so many of the diseases of the NIAMS, will undoubtedly benefit from the Institute's growing research efforts and the special education initiatives NIAMS is currently implementing in lupus and osteoporosis.

Purpose and Method of Operation

Extramural research and training are supported through five program areas: arthritis, bone biology and bone diseases, musculoskeletal diseases, muscle biology, and skin diseases. Funding mechanisms include research project grants, research centers, other research grants, research training, and research and development contracts. Intramural research is conducted at three research laboratories and one clinical research branch. The leadership and scientific direction of the Institute are funded through the activity entitled Research Management and Support.

Funding for the National Institute of Arthritis and Musculoskeletal and Skin Diseases during the last five years has been as follows:

	Amount	FTE
FY 1988	$ 147,543,000	104
FY 1989	159,886,000	113
FY 1990	168,563,000	118
FY 1991	193,466,000	138
FY 1992	203,913,000	141

Overall Budget Policy

The FY 1993 budget request for the National Institute of Arthritis and Musculoskeletal and Skin Diseases is $214,929,000, an increase of $11,016,000 over the comparable 1992 level of $203,913,000.

The request includes 146 FTEs, an increase of five FTEs over the FY 1992 level of 141. The additional FTEs will allow the NIAMS to continue to support activities begun in FY 1992 and will provide support for the expansion in the areas of bone biology and bone diseases and arthritis and related musculoskeletal diseases. Intramurally, additional FTEs will be provided for the Laboratory of Structural Biology and the Laboratory of Skin Biology.

At the FY 1993 request level, the Institute will support 562 noncompeting research project grants at $110,538,000 and 184 competing grants at $36,778,000 compared to 529 and 194, respectively, in 1992.

The FY 1993 request includes $22,961,000 for 28 research centers, $6,725,000 for other research, $6,854,000 for research training, and $4,018,000 for R&D contracts; the same as the 1992 level.

Intramural research will be conducted at a level of $16,550,000 and 75 FTEs, compared with $15,753,000 and 72 FTEs in FY 1992.

Research management and support activities will be funded at $9,855,000 and 71 FTEs, compared to $9,395,000 and 69 FTEs in FY 1992.

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Arthritis and Musculoskeletal and Skin Diseases

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite.

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$169,895,000	$178,765,000	$188,524,000	+$9,759,000

The Institute has primary responsibility at the National Institutes of Health for extramural research and research training in arthritis, bone biology and bone diseases, musculoskeletal diseases, muscle biology and skin diseases.

Funding for the Arthritis and Musculoskeletal and Skin Diseases Program during the last five years has been as follows:

	Amount
FY 1988	$133,677,000
FY 1989	144,560,000
FY 1990	149,018,000
FY 1991	169,895,000
FY 1992	178,765,000

Rationale for the Budget Request

The FY 1993 budget request for the Arthritis and Musculoskeletal and Skin Diseases Program is $188,524,000, an increase of $9,759,000 over $178,765,000 for FY 1992. The following are examples of current research activities and plans for FY 1993.

Rheumatoid Arthritis

Afflicting over two million Americans, rheumatoid arthritis is a major crippling disorder of the joints. In serious cases, the disease process goes well beyond joint pain and destruction; it also causes inflammation in the blood vessels and other vital organs. Much has been learned about the highly coordinated events surrounding the characteristic inflammation of rheumatoid arthritis. It is now possible to identify the genetic elements involved, to understand the migration of white blood cells crucial to the immune defenses to the site of joint inflammation, and to explain "molecular mimicry" (the sharing of antigens by both bacterial and human cells). The Institute is actively pursuing basic research in an effort to establish a clearer linkage between the genetic, immunologic, and environmental factors that underlie this disease, that affects women to a much greater extent than men.

As detailed knowledge of the abnormal immune processes of rheumatoid arthritis appears, scientists have focused on the central role of the CD4 (immune helper) cells and on the release of the inflammatory agent IL2 by triggering a cell receptor called IL2R. Now scientists are trying new therapies based on selectively killing the CD4 cells or on blocking the IL2R receptor.

To destroy joints, cells of tissues lining or invading the joints release highly specific enzymes (proteinases) that eat away cartilage and bone. If these enzymes can be inhibited, joint damage will not occur. NIAMS scientists are actively tracking the sites in which these enzymes are made, the circumstances under which they are released or activated, and the methods by which they can be inactivated. Success will mean the creation of an entirely new form of therapy.

Pediatric Rheumatic Diseases

Rheumatic diseases of childhood afflict thousands of children in the United States and include several diseases associated with arthritis and related musculoskeletal syndromes. These include rheumatoid arthritis, spondyloarthropathies, lupus, scleroderma, and others. Juvenile rheumatoid arthritis (JRA), characterized by chronic joint inflammation, remains predominant; more than half of the children with pediatric rheumatic diseases are affected by JRA.

NIAMS is interested in building on the emerging understanding of how genetic factors confer susceptibility to JRA, as well as enhancing research on the immune system and how the interplay of hormonal and immunologic factors gives rise to inflammation and tissue destruction. More specifically, the Institute is pursuing research on elements of the immune system (cytokines) that occur at local sites of inflammation, abnormal antibodies present in the blood of patients with various types of JRA, and therapies that will counteract the effects of JRA on bone growth and development. Investigators are searching for several viruses in the joints of children with JRA to better understand the pathogenesis of the disease.

Lupus

Lupus is a chronic, inflammatory autoimmune disease that occurs in two forms: systemic and discoid. Systemic lupus can affect various internal organs and be life-threatening. It often begins with arthritis. Skin rash is the main feature of discoid lupus--a more benign but disfiguring disorder.

To better understand why the immune system goes awry in patients with systemic lupus, the Institute is pursuing research on the regulatory abnormalities of the white blood cells that orchestrate immunodefenses (T cells), the increased rates of gene mutations that give rise to abnormal antibodies, and the pathogenic steps that lead from antibody deposition to destruction of tissue. Other areas include the search for new pathogenic infectious agents and the elucidation of mechanisms of drug action that could result in improved therapy for lupus patients--especially those with severe disease.

Many of the people in the United States who are afflicted with systemic lupus are women of childbearing age. Many pregnant women with lupus lose their babies, and it is known that the immune system is involved. In September 1991, NIAMS and NHLBI sponsored a conference on antiphospholipid antibody/lupus anticoagulant. Following the meeting, the two institutes issued a program announcement to stimulate research on the mechanisms of action of these two closely related abnormal antibodies. Areas of study being encouraged include defining differences and similarities, developing animal models, and conducting clinical studies and treatment trials.

The Institute held a major 3-day workshop on lupus in January 1992. The goal of this question-driven workshop was to set a new research agenda for lupus. Lupus has a three times higher incidence, prevalence, and mortality in black women than in white women; the reasons for this anomaly are unknown. Workshop participants gave careful consideration to this question, as well as others related to immunologic, genetic, and environmental factors believed to be at the cause of lupus.

Working with the Task Force on Lupus in High Risk Populations, which the Institute established in recent years, NIAMS has created a lupus resource kit designed to assist organizations and community leaders in raising awareness about lupus. Included in the kit are educational materials, suggested activities, and a highly effective booklet for the public entitled "What Black Women Should Know About Lupus." Future efforts will focus on enhanced outreach to health professionals and, later, to other minorities who suffer from lupus.

Osteoarthritis

Osteoarthritis, or degenerative joint disease, is caused by progressive deterioration of cartilage and overgrowth of bone. It is the most common form of arthritis, affecting some 16 million Americans. About one-third of all adults in the United States have radiographic evidence of osteoarthritis in at least one part of the body by 65 years of age.

Several biochemical and biomechanical changes have been discovered as the disease progresses. However, the factors leading to initial deterioration and to rapid degeneration in later stages are not well understood. Investigations into the roles of recently identified noncollagenous proteins in cartilage could provide insight into cartilage metabolism and macromolecular organization. Additional research opportunities are afforded by powerful imaging technologies such as MRI, which can be used to study cartilage damage at earlier stages. Increased knowledge about its breakdown and repair should lead to a better understanding of the disease process in osteoarthritis and to more effective interventions.

Scleroderma

Systemic sclerosis, commonly called scleroderma, literally means "hard skin." It is a disease of connective tissue and small blood vessels, notably in the skin. Overproduction of collagen, a major protein of connective tissue, causes the skin to thicken and harden. When the vascular disease occurs in vital organs such as the lungs, heart, and kidneys, there can be life-threatening complications. The disease usually begins between ages 30 and 50, and the incidence in women is about four times that in men.

Although the exact cause of scleroderma is unknown, at least three factors appear to be involved: (1) excessive deposit of collagen in skin and internal organs, (2) vascular lesions in capillaries and small arteries, and (3) immunologic abnormalities. At present, it is not clear which of these factors is of primary importance. In October 1991, the Institute sponsored a conference on acquired connective tissue diseases, which included in-depth discussions of scleroderma. One of the new concepts to emerge from the conference concerned mast cells (which play a role in allergic responses) and their likely involvement in the fibrotic process. Therapeutic modulation of mast cells may aid in treating scleroderma; NIAMS is pursuing this lead.

Other basic research is aimed at determining whether collagen-producing cells (fibroblasts) in patients with scleroderma function autonomously or are dependent upon signals generated by the immune system. Working at the molecular level, researchers are defining factors that control the fibroblast gene and regulate the synthesis and growth of collagens. Elucidation of the role of T cells (small white cells that orchestrate immune defenses) in the initiation or perpetuation of the disease is also being examined.

To enhance treatment, the Institute is focusing on epidemiologic studies to identify environmental triggers for scleroderma and scleroderma-like syndromes and on improving clinical, immunologic, and genetic subtyping of scleroderma syndromes.

Lyme Disease

The infection known as Lyme disease is spreading beyond the well-known endemic areas in this Nation (the Northeast, upper Midwest, and Northern California); 46 out of 50 states have now reported cases. Recently, birds were shown to carry the ticks for long distances, perhaps accounting for the geographic spread. As Americans take to woodsy areas for recreation or work, they risk exposure to the bacterium--carried by ticks--that causes Lyme disease.

NIAMS is pursuing research aimed at improving diagnosis, treatment, and prevention of Lyme disease. Scientists are working on developing rapid tests for antigens of the causative bacterium; diagnostic criteria in children and adults; the utility of various biological fluids and tissues for diagnosis; the appropriate treatment of the disease in children, adults, and pregnant women; the utility of prophylactic antibiotics in exposed individuals from endemic areas, and a Lyme vaccine.

Muscle Exercise Physiology

The metabolism and protein composition of skeletal muscle change profoundly either by increased exercise or after immobilization and in space travel. Recent research indicates that scientists are at the cutting edge of being able to characterize and understand both use and disuse feedback. This should enable them to determine factors that underlie muscle wasting, elucidate mechanisms by which the use of corticosteroids contributes to muscle atrophy, and conduct clinical trials to assess activities that may be helpful to prevent muscle injury and atrophy. These studies will also add to our knowledge of the problems experienced by the physically active American public, such as weekend athletes.

Biological Markers of Osteoporosis

Osteoporosis is a condition of low bone mass leading to bone fractures. It is a major public health problem in the United States. Technical advances in bone mass measurement have improved the ability to determine who is at risk of osteoporotic fracture. However, detectable changes in bone turnover occur slowly over years, creating a need for the development of biochemical markers that accurately reflect early changes in bone turnover to improve prediction of those at risk of fracture and to assess the results of treatment. Most useful are substances that appear in the blood and urine that are specific products of either osteoblastic or osteoclastic activity.

Two major studies of osteoporosis are being launched this year: the NIH Women's Health Initiative (WHI) intervention and observational study, and a World Health Organization (WHO) project. NIAMS, the lead institute in osteoporosis research, is playing a major role in the planning of both studies. Prior to their initiation, the Institute held a workshop on Biochemical Markers of Bone Remodeling in Osteoporosis in December 1991. The workshop was extremely productive. Participants agreed that certain markers of bone turnover are of particular value in identifying persons at risk of developing osteoporosis before the disease is detectable by bone measurement. These biochemical markers have the potential to detect whether women in early menopause are undergoing excessive bone remodeling that is likely to result in excessive bone loss. If this is the case, intervention can be initiated early in the process.

Cost-Effective Strategies for the Treatment, Diagnosis, Bone Remodeling, and Prevention of Osteoporosis

The debilitating degenerative bone disorder of osteoporosis affects over 25 million Americans, mainly women 4 to 1. The resultant fractures cause great pain and disability, as well as extensive hospital and rehabilitation costs. The Senate Appropriations Report of 1991 contained language requesting the conduct of research related to identifying and evaluating cost-effective strategies for prevention, diagnosis, and treatment of osteoporosis and related bone disorders. NIAMS, together with the Agency for Health Care Policy and Research, will hold a workshop to define the agenda for assessing these costs.

Musculoskeletal Fitness and Sports Injuries

The contributions of muscles and other supporting connective tissue structures (tendons, ligaments) to joint stability and function are not fully defined. Increasing participation in sports and exercise programs warrants enhanced research efforts in this area. Studies are planned to determine the effect of motion and stress on musculoskeletal tissue, the factors involved in the regeneration of bone and muscle tissue, and the most effective treatment for specific anatomic problems such as damaged ligaments. The Institute also plans to assess sports injuries in children and the need for surveillance data in order to develop effective preventive strategies.

In connection with repair of sports injuries (and other musculoskeletal disorders), the Institute is supporting research on biomaterials to improve the effectiveness of prostheses. Researchers are investigating the interrelationships between biomaterial implants and inflammation, infection, wound healing, repair, and degradation. They are examining the host-device response mechanism. They are also investigating processes to improve the porous-surface structure of orthopaedic implants to optimize their ability to permit bone ingrowth subsequent to implantation. The purpose of this effort is to gain the knowledge necessary to develop more effective long-term orthopaedic implants and improve the quality of life for implant recipients.

Repetitive Motion Syndrome

Repetitive motion injuries account for half of the Nation's occupational illnesses. Affected workers are employed in many different segments of industry; however, they are concentrated in situations that require repeated heavy loading or light loading in awkward positions. More information is needed on mechanisms by which a repeated motion causes mechanical disruption and biochemical alteration of connective tissue. NIAMS is currently supporting research on the effects of mechanical loading at varied levels to determine cell response. The Institute is also amassing data on the occurrence of repetitive motion syndrome, investigating treatment approaches, and exploring preventive measures.

Pemphigus Foliaceus

Pemphigus is a group of severe, often fatal blistering diseases that affect the skin and mucous membranes. These are autoimmune disorders that involve attachment of antibodies to desmosomes, proteins that connect epidermal cells together. One particular type of pemphigus, endemic pemphigus foliaceus, is native to Brazil. Those afflicted with this devastating fatal disease are concentrated in homes along rivers that are heavily infested with black flies. NIAMS scientists are intensively searching for a causative microorganism that initiates this autoimmune disease, in the expectation that lessons learned from pemphigus foliaceus will be applicable to patients with other forms of pemphigus.

Epidermolysis Bullosa

Groundbreaking research in epidermolysis bullosa (EB), a set of devastating blistering diseases, has revealed the molecular bases for the disintegration of the skin in two forms of the disease. In EB simplex, defects in the genes for keratin (the most abundant protein in cells of the outer layer of skin, the epidermis) were found. In dominant dystrophic EB, a mutation was identified in the gene for type VII collagen, the protein that anchors the epidermis to the inner layer of the skin, the dermis. Determining the genetic basis for different forms of EB is a prelude to the development of specific therapies.

Chronic Wounds

Chronic wounds in the elderly and those confined to chronic care hospitals represent a major public health problem. There has been much recent interest--in the pharmaceutical industry and elsewhere--in wound dressings and the stimulation of wound healing; much of this work, however, has been based on treatment in acute, rather than chronic, wounding models. NIAMS and four other NIH components are planning to hold a workshop on the Pathogenesis of Chronic Wound Healing in the fall of 1992. Participants will review acute and chronic wound healing; compare decubitus, diabetic, and venous wounds; examine the control of tissue that supports the skin and prepares it for solid healing dermal/epidermal interaction; and formulate specific recommendations for future research.

Skin Manifestations of Lyme Disease

Lyme disease has both arthritis and skin disease among its many manifestations. There has been a considerable amount of research on the arthritis of Lyme disease, but the skin manifestations of Lyme disease--which are part of both the acute and chronic forms of the disease--have not been fully studied. NIAMS plans to stimulate research on the skin manifestation of Lyme disease in an effort to improve possibilities for intervention.

Skin Cancer

An estimated 600,000 Americans will be diagnosed with skin cancer this year, and the incidence of melanoma is rising rapidly. If not diagnosed and treated promptly, it is often fatal. Although increased surveillance, along with early intervention, has the potential to provide greatly improved cure rates, it has become increasingly clear that agreement regarding specific histologic criteria for early diagnosis is lacking. Furthermore, the American people need to recognize the necessity for early diagnosis and treatment.

NIAMS-supported researchers are investigating a number of questions in dermatology to understand the development of various skin cancers, including basal and squamous cell carcinomas and melanoma. Some investigators are studying the effects of ultraviolet (UV) light on immune cells found in the skin. Other investigations focus on how UV light damages genetic material in cells, thus initiating the process of carcinogenesis. Studies of diseases like psoriasis and vitiligo are also revealing information that has potential importance for understanding skin cancer. Psoriasis, like skin cancer, involves the rapid proliferation of skin cells. Researchers may uncover important findings relative to skin cancer as they make discoveries about the mechanisms of psoriatic cell proliferation. Vitiligo involves the abrupt self-destruction of pigment-forming cells of the skin, melanocytes. An understanding of how these cells are turned off may help researchers control the rapid overgrowth of these same cells when they take the form of a deadly skin cancer called melanoma.

NIAMS is collaborating with the National Cancer Institute in planning the NIH Consensus Development Conference on the Diagnosis and Treatment of Early Melanoma, which was held in January 1992. It will bring together experts in the fields of dermatology, pathology, epidemiology, public education, and surveillance techniques--as well as representatives of the public--to explore the data and evaluate the current technology for diagnosis and treatment of this disease.

HIV/AIDS

The Institute is planning a population-based study of the arthritic and skin manifestations of HIV infection. These manifestations may occur early in the course of HIV infection and cause considerable morbidity. The aim of this new initiative is to enhance understanding of how interaction of the immunosuppressive and infectious processes produce rheumatic disease in HIV-infected individuals.

Because differences have been found in the clinical spectrum and course of HIV infection when comparing community-based and hospital-based populations, the Institute wishes to extend the scope of data currently being accrued in Army and Navy populations. The planned, community-based studies will emphasize women, minorities, and intravenous drug users. The knowledge obtained may provide a rationale for interventions to treat or prevent cutaneous and rheumatic morbidity associated with HIV infection.

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Intramural Research Program

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite.

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
69	$14,491,000	72	$15,753,000	75	$16,550,000	+3	+$797,000

The Intramural Research Program of the NIAMS conducts basic and clinical research and research training in the diseases within the mandate of the Institute. Within the Arthritis and Rheumatism Branch, basic and clinical research has contributed to both the understanding of these diseases and the understanding of the researchers in the Laboratory of Physical Biology study biological problems using a broad range of physical techniques.

The recently established Laboratory of Skin Biology studies proteins important for the differentiation of the skin and has added a program of medical genetics to pursue studies of keratinizing disorders such as the ichthyoses and psoriasis.

Another new intramural component, the Laboratory of Structural Biology studies the macromolecular aspects of differentiating skin, muscle fibers, cell membrane proteins, and viral particles.

Funding for Intramural Program during the last five years has been as follows:

	Amount	FTE
FY 1988	$ 8,756,000	47
FY 1989	9,572,000	53
FY 1990	12,062,000	55
FY 1991	14,491,000	69
FY 1992	15,753,000	72

Rationale for the Budget Request

The FY 1993 budget request for the Intramural Program is $16,550,000, an increase of $797,000 over the FY 1992 estimate of $15,753,000.

The following are examples of research activities being carried out in the NIAMS Intramural Research Program:

Mediators of Inflammation

Intramural researchers continue their studies of a cell surface receptor that has high affinity for immunoglobulin E, one of five serum proteins that include all known antibodies. This receptor has far-reaching medical significance because it is important in triggering allergic reactions (and inflammation) whenever the immunoglobulin E that is bound to it reacts with antigen. Currently, investigators are attempting to gain insight into how this receptor initiates the allergic response. Such information can form the basis for developing new specific drugs to block immunoglobulin E-mediated allergies and inflammation.

Inflammatory Myopathies

Inflammatory myopathies (polymyositis, dermatomyositis, and related disorders) are a family of muscle diseases causing severe muscle weakness and in some, death. Many patients with such myopathies respond poorly to therapy with corticosteroids. Intramural scientists have demonstrated that one form of myositis has a seasonal occurrence, suggesting an infectious cause. They have undertaken several therapeutic trials to improve treatment of such patients. The current trial is determining whether methotrexate (an immunosuppressive drug) given intravenously or in combination with azathioprine (another immunosuppressive drug) improves the course of disease. Future plans include a clinical trial of a promising bioengineered antibody.

Muscle Force Generation

A widely accepted model of muscle contraction is that force is generated when two major proteins, myosin and actin, interact with each other. These proteins make up the so-called thick and thin filaments of muscle, respectively. The arrangement of crossbridges between these two filaments suggests that the thick filaments pull the thin filaments by a kind of ratchet (or "rocking") action of the crossbridges.

Many investigators over the years have attempted--without success--to detect crossbridge rocking in muscle fibers. Last year, for the first time, NIAMS intramural scientists were able to produce such molecular movement that was detectable by x-ray signal. By pretreating muscle fibers with a chemical that caused the crossbridges between the thick and thin filaments to remain weakly attached, they found this year that the rotatability of weakly binding crossbridges differs from that of strongly binding crossbridges. This indicates that force is generated by a transition between these two states, thus providing evidence that attached crossbridges are essential for force generation in skeletal muscle.

Laboratory of Structural Biology Research

Researchers in the Laboratory of Structural Biology Research (LSBR) are investigating mechanisms of molecular assembly and structure-function relationships using high resolution electron microscopy in conjunction with computer imaging. Systems of interest are the structure of viruses, intermediate filaments including keratins (epithelial and epidermal structures), and the proteinaceous fibers that form much of the connective tissue found in cartilage, muscle, and skin. One of the viruses being studied is the AIDS virus with a focus on the structural organization of the surface glycoproteins. This research will enhance knowledge of the relationship between the infectivity of the virus and its physical structure, advancing the mission for vaccine development.

The x-ray crystallography group is enhancing the laboratory's capabilities with regard to high-resolution structural studies of multienzyme complexes and other macromolecular complexes. Such high-resolution studies will enable researchers to view a direct representation of life at the molecular level in tissues affected by the diseases under the mandate of the Institute.

Laboratory of Skin Biology

Established in the spring of 1990, the Laboratory of Skin Biology (LSB) performs research on the principal proteins of the epidermis, the skin's outer layer. The LSB has a strong section in molecular biology and structure; it recently unveiled the assembly of keratin intermediate filament chains. These filaments are expressed in terminally differentiated epidermal cells, those that are turning into the flattened, outermost skin cells that provide a barrier function for the skin. The new laboratory is also investigating the genetics underlying inherited keratinizing disorders, including the ichthyoses.

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Research Management and Support

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite.

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
69	$9,080,000	69	$9,395,000	71	$9,855,000	+2	+$460,000

This activity provides the staff and resources for the scientific leadership and overall management and direction of the entire Institute. It includes the staffs of Office of the Director and of the Extramural Program activities; and involves a wide range of functions, including administration, evaluating research needs, selecting promising research areas for new or expanded investigation and implementing new initiatives. Also supported are Institute data systems, public information activities, and management of the Institute's diverse grant portfolio.

Funding for Research Management and Support during the last five years has been as following:

	Amount	FTE
FY 1988	$5,110,000	57
FY 1989	5,754,000	60
FY 1990	7,486,000	63
FY 1991	9,080,000	69
FY 1992	9,395,000	69

Rationale for the Budget Request

The FY 1993 budget request for Research Management and Support is $9,855,000, an increase of $460,000 over the FY 1992 estimate of $9,395,000. The following are examples of research activities funded in Research Management and Support.

The Office of the Director provides the guidance and professional leadership for all the Institute's programs. It includes four main staff offices: the Office of Administrative Management; the Office of Program Planning and Evaluation (OPPE); the Office of Scientific and Health Communications (OSHC); and the Office of Prevention, Epidemiology and Clinical Applications (OPECA),

The Office of Scientific and Health Communications serves as the focus of most of the public information, and the health, patient, and professional education efforts of the Institute. It also plans, implements and manages major information/education efforts such as the National Arthritis and

Musculoskeletal and Skin Diseases Information Clearinghouse and the Task Force on Lupus in High Risk Populations. Through OSHC, NIAMS is enhancing its prevention and education efforts on osteoporosis and related bone disorders. The Institute plans to award a contract for an osteoporosis and related bone disorders resource center and to distribute an Osteoporosis Prevention and Education Resource Guide, prepared by OSCH staff.

The Office of Prevention, Epidemiology and Clinical Applications develops and coordinates Institute policies and programs of disease prevention and health promotion, epidemiology and biometry, technology assessment and transfer, and clinical studies and trials.

The Extramural Program staff are responsible for administration of the Institute's research grant activities. Scientific staff engage in planning and development of programs designed to stimulate important research, administer grants and contracts, and provide guidance on scientific programs and ensure dissemination of research results to the scientific community and the public.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Detail of Permanent Positions

	1991 Actual	1992 Appropriation	1993 Estimate
ES-5	1	1	1
ES-4	2	2	2
ES-2	1	1	1
GS/GM-15	12	13	13
GS/GM-14	11	12	13
GS/GM-13	7	8	11
GS-12	10	11	11
GS-11	6	6	6
GS-10	1	1	1
GS-09	6	6	7
GS-08	4	4	3
GS-07	21	21	21
GS-06	5	5	5
GS-05	6	5	5
GS-04	6	6	6
Subtotal	99	102	106
Grades established by act of July 1, 1944 (42 U.S.C. 207):			
Surgeon General Grade	0	0	0
Asst. Surgeon General Grade	0	0	0
Director Grade	7	7	7
Senior Grade	2	3	3
Full Grade	0	0	0
Senior Assistant Grade	5	5	6
Subtotal	14	15	16
Ungraded	1	0	0
Total permanent	114	117	122

NATIONAL INSTITUTES OF HEALTH

National Insitute of Arthritis and Musculoskeletal and Skin Diseases
New Positions Requested

	Grade	1993 Number	1993 Annual Salary
Intramural Research			
Medical Officer	CO-06	1	$ 56,775
Molecular Biologist	GS-14	1	54,607
Molecular Biologist	GS-13	1	46,210
Subtotal		3	$157,592
Research Management and Support			
Health Scientist Administrator	GS-13	2	$ 92,420
Subtotal		2	$ 92,420
Total		5	$250,012

AMOUNTS BUDGETED FOR INCREASES IN
FULL-TIME EQUIVALENTS

ACTIVITY/POSITIONS	GRADE	NO. OF POS.	O.C. 11 ANNUAL SALARY	O.C. 12 BENEFITS 19.0%	O.C. 21 TRAVEL	O.C. 23.1, 23.2 RENT	O.C. 23.3 COMM/ UTIL	O.C. 25 OTHER SERVICE	O.C. 31 EQUIPT.	OTHER OBJECTS	SUB.TOT. NEW COSTS	SUPPOT STAFF SHARE	NO. OF FTE	TOTAL NEW COSTS
NIAMS Intramural Research														
Medical Officer	CO-06	1	56,775	10,787	1,000			2,000		100	70,662		1.00	70,662
Molecular Biologist	GS-14	1	54,607	10,375	1,000			2,000		100	68,082		1.00	68,082
Molecular Biologist	GS-13	1	46,210	8,780	1,000			2,000		100	58,090		1.00	58,090
		3	157,592	29,942	3,000	0	0	6,000	0	300	196,834	0	3	196,834
NIAMS Research Management and Support														
Health Scientist Administrator	GS-13	1	46,210	8,780	3,500			2,000		100	60,590		1.00	60,590
Health Scientist Administrator	GS-13	1	46,210	8,780	3,500			2,000		100	60,590		1.00	60,590
		2	92,420	17,560	7,000	0	0	4,000	0	200	121,180	0	2	121,180
Total		5	250,012	47,502	10,000	0	0	10,000	0	500	318,014	0	5	318,014

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Increases in Positions

Additional positions are requested to pursue research opportunities in high priority areas, such as bone biology and bone diseases; structural biology of connective tissues, muscle, and skin; molecular genetics of skin; and the various forms of arthritis and related musculoskeletal diseases.

The NIAMS would hire molecular biologists and a medical officer to investigate the structural biology of connective tissues, muscle and skin, and the molecular genetics and epidermal differentiation of skin.

The NIAMS would hire health scientist administrators to respond to expanding scientific opportunities and national interest in the various forms of arthritis and related musculoskeletal diseases and the scientific bases that underlie the clinical manifestations of these diseases, and in bone biology and bone diseases, especially osteoporosis.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Advisory and Assistance Services

Consultant services continue to be of critical importance in carrying out the mandates under which we operate. The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) use of consultant services is for the National Advisory Council, the National Advisory Board, and the Board of Scientific Counselors. The appointed members of these congressionally mandated groups provide scientific, medical, and technical expertise to the Institute and perform services that are essential to the review process; by statute, their concurrence is required before most grant awards can be made (section 475 of the Public Health Service Act, 42 USC 289 1-4).

The cost of consultant services decreased from $138,000 in fiscal year 1991 to $53,000 in fiscal year 1992, a net decrease of $85,000. In fiscal year 1991, the NIAMS spent $117,000 to convene a series of task forces to develop a National Research Plan.

The cost of consultant services increased from $53,000 in FY 1992 to $55,000 in FY 1993, an increase of $2,000 which reflects the continued support of the National Advisory Council, the National Advisory Board, and the Board of Scientific Counselors.

Policy guidelines for internal controls exist in the form of OMB Circular A-120 and DHHS General Administration Manual 8-15. Each year a consultant services plan is prepared identifying planned Advisory and Assistance Services procurement. The NIH accounting system contains Common Account Numbers (CANS) that have been designated for use in identifying and aggregating costs for Advisory and Assistance Services.

TUESDAY, MARCH 24, 1992.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

WITNESSES

DR. RUTH L. KIRSCHSTEIN, DIRECTOR, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

DR. JAY MOSKOWITZ, ASSOCIATE DIRECTOR FOR SCIENCE POLICY AND LEGISLATION, NATIONAL INSTITUTES OF HEALTH

DR. MARVIN CASSMAN, DEPUTY DIRECTOR, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

G. EARL HODGKINS, FINANCIAL MANAGEMENT OFFICER, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

DR. W. SUE SHAFER, ASSOCIATE DIRECTOR FOR PROGRAM ACTIVITIES, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

MARTHA PINE, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

DENNIS P. WILLIAMS, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTRODUCTION OF WITNESSES

Mr. NATCHER. At this time we take up the budget request for the Institute of General Medical Sciences.

We have before the Committee Dr. Ruth L. Kirschstein, the Director.

Dr. Kirschstein, it is a pleasure to have you back before our Committee, not only because we like you and you are doing a good job, but because you are the senior member out there at NIH.

Dr. Kirschstein, you take care of yourself. We want you to be out there a long time. I am going to stay awhile with you.

Before you leave, Dr. Kirschstein, look at your picture over here. We have it hanging on the wall.

I believe it was the first picture I have ever seen of all the Institute Directors. We thought enough of you and the others to put it on the wall.

We are glad to have you.

Before you give us your statement, tell us who you have with you at the table.

Dr. KIRSCHSTEIN. Good morning.

Thank you for the comments. In the 17 or 18 years I have been at this, that is the first time such a picture has been taken. We are very grateful to you for that.

I have with me Dr. W. Sue Shafer, Associate Director for Program Activities of the Institute; next to her, Mr. Earl Hodgkins, the Budget Officer; next to him, Ms. Martha Pine, the Executive Officer. You will recall that last year, Ms. Pine was unable to be with us. We are very pleased she is with us this year.

To my right is Dr. Marvin Cassman, the Deputy Director of the Institute; to his right, Dr. Moskowitz, the Associate Director of the NIH; and to his right, Mr. Dennis Williams, the Deputy Assistant Secretary for Budget.

Mr. NATCHER. Thank you.

We will be pleased to hear from you.

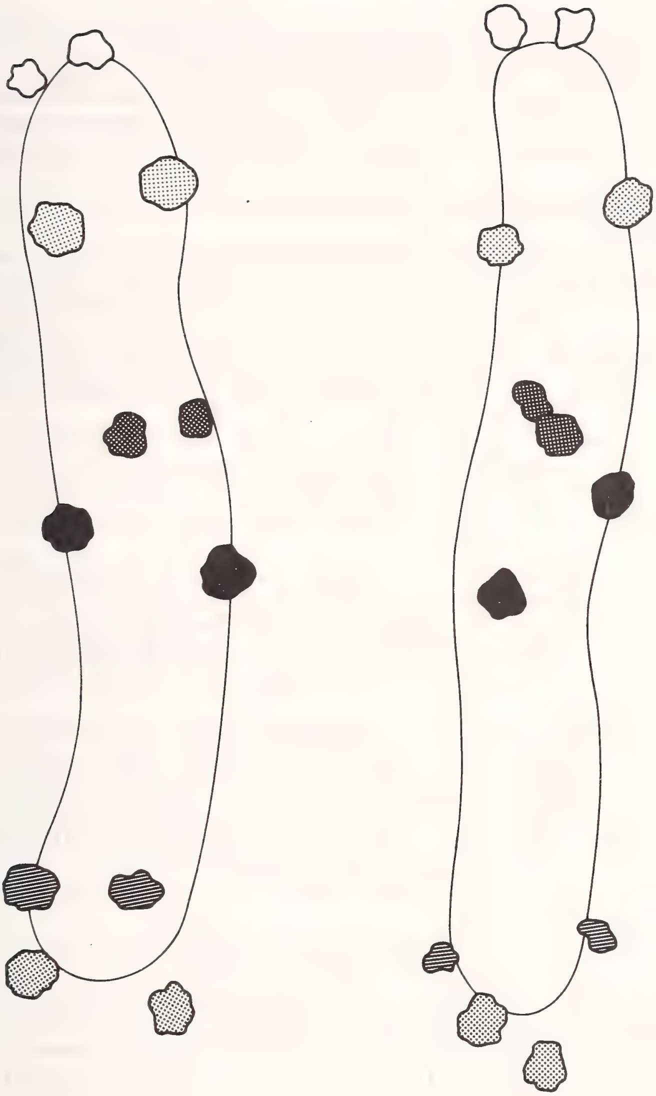
OPENING STATEMENT

Dr. KIRSCHSTEIN. Good morning, Mr. Chairman, and members of the Committee. I am delighted to have the opportunity, once again, to present to you the outstanding programs and achievements of the National Institute of General Medical Sciences, NIGMS. NIGMS grantees are at the forefront of such fields as genetics, molecular biology, chemistry, structural biology, and pharmacology. The Institute is a leader in the support of research related to biotechnology.

A very exciting technology, developed by Dr. David Ward of Yale University, is called high-resolution fluorescence *in situ* hybridization. Using different fluorescent tags to label pieces of DNA, Dr. Ward can "paint" specific chromosomes.

Here is a photograph of human chromosome number 5 showing six different DNA segments, each lighting up as a different color.

[The information follows:]



Simultaneous detection of six DNA sequences on human chromosome 5. The research was led by Dr. David Ward of Yale University, with support from the National Institute of General Medical Sciences.

Using one application, Dr. Ward can detect additions, deletions, duplications, and rearrangements of genetic material, any of which may be associated with genetic diseases or malignancies.

Such a technology could increase the speed and accuracy—and reduce the cost—of detecting and locating specific genetic sequences, thus aiding in diagnosis of inherited diseases, as well as malignancies.

I have provided copies of this photograph for each of the Committee Members.

Another new biotechnological advance is an important variation of the polymerase chain reaction. This co-called ligase chain reaction amplifies the DNA and was developed by an NIGMS grantee. The ligase chain reaction allows the detection of extremely small changes in DNA sequences, thus also holding great promise for increasing the accuracy and availability of diagnostic tests for a number of diseases, particularly inherited disorders.

As you know, NIGMS plays a pivotal role in the support of research that determines molecular structures at high resolution. Much of our current understanding of the detailed mechanisms by which biological molecules function has come from studies in this field of structural biology.

This year, a scientific team led by Dr. David Matthews of Agouron, a California biotechnology company, determined the three-dimensional structure of Ribonuclease H, or RNase H, a protein that is critical to the life cycle of the AIDS virus. Knowledge of this structure could provide a valuable target for the rational design of anti-AIDS drugs.

NIGMS also approaches drug design through its substantial support of basic research in chemistry, especially work aimed at the synthesis of natural products and new drugs. It is clear that, increasingly, work at the chemistry-biology interface will become more and more important to the biotechnology and pharmaceutical industries, and this country must have an adequate number of highly-trained, creative, skilled scientists in this area to remain competitive in these arenas.

As you know, the Institute has two longstanding activities, the Minority Access to Research Careers (MARC) and the Minority Biomedical Research Support (MBRS) programs, designed to rectify the underrepresentation of minority groups in biomedical research.

This year, with funds provided by the Congress, we have started a new national program of individual predoctoral fellowships for minority students. One hundred and one such fellowships were awarded at the end of fiscal year 1991 to minority students in graduate schools across the country.

We were so pleased with last year's response to this new program that we have issued another call for applications and, with the cooperation of a number of other NIH components, we plan to make further awards this fiscal year.

Mr. Chairman, later this year, NIGMS will celebrate its 30th anniversary. We are proud of the many accomplishments we have made possible, and we know that the solid base of knowledge and the highly-qualified, highly-skilled, new scientists we have trained will continue to speed the pace of discoveries in the years ahead.

NIGMS is $862,069,000.

I would be pleased to answer any questions you might have.

[The statement of Dr. Kirschstein follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement of the Director
National Institute of General Medical Sciences

Mr. Chairman and Members of the Committee, good morning. I am delighted to have the opportunity, once again, to present to you the outstanding programs and achievements of the National Institute of General Medical Sciences (NIGMS). The NIGMS supports basic, non-disease-targeted research that forms the foundation for clinical advances. NIGMS grantees are at the forefront of such fields as genetics, molecular biology, chemistry, structural biology, and pharmacology. The Institute is a leader at NIH in the support of research related to biotechnology as well as the support of programs designed to increase the number of biomedical scientists.

Year after year, the Institute's research programs yield significant new findings that shape scientific thought. In times of tight budgets, the basic research supported by NIGMS may prove to be the most effective use of funds, because basic findings have broad applications to many clinical problems and to industrial needs. It is no accident that NIGMS supports so much Nobel Prize-winning research, because Nobels are awarded for the sort of seminal work that the Institute funds.

Let me give you a few examples. In the late 1970's, an NIGMS grantee, Dr. Alfred Gilman, discovered proteins involved in the cell's response to light, hormones, drugs, neurotransmitters, and other outside signals. Dr. Gilman, who is now at the University of Texas Health Science Center at Dallas, named them "G proteins," after the DNA building block, guanine, to which they bind. Since Dr. Gilman's original discovery, he and other scientists have found many more G proteins and have begun to explore the tantalizing clues linking these proteins to cancer, diabetes, high blood pressure, and other disorders.

Another group of NIGMS-supported scientists has recently made a major finding in the field of genetics. Their work sheds light on transposable elements, the somewhat mysterious segments of DNA that move around the genetic material of an organism. The identification of these elements by Dr. Barbara McClintock of the Cold Spring Harbor Laboratory was honored with a Nobel Prize in 1983. Dr. McClintock worked with corn genes; other scientists have since observed the movement of transposable elements in various organisms, but not in humans or in other mammals. Now, a team led by Dr. Haig Kazazian of the Johns Hopkins University School of Medicine has identified a human transposable element that moved from one location in the genome of a child's parent to a new location in the genome of the child. They have also demonstrated that movement of the element is involved in a genetic disease, in this case, hemophilia. A second group at Hopkins has shown that the transposable element contains a segment that codes for the reverse transcriptase enzyme, which is involved in the movement of DNA segments around the genome, as well as in the incorporation of certain viruses, such as HIV, into an organism's genome. These discoveries should advance understanding of how transposable elements arose and, more importantly, of how they work.

A third example is found in the work of Dr. Gerald Fink of the Whitehead Institute for Biomedical Research, who has been supported by NIGMS for over 20 years to do very basic studies on the growth of yeast. Dr. Fink has discovered a way to make a non-disease-causing form of yeast undergo an unexpected change in shape, from a round cell to a long, thread-like filament. The mechanism by which this change occurs is thought to be similar, if not identical, to the mechanisms that enable other types of yeast, such as Candida albicans, to cause disease. Because the shape change can now be controlled in the laboratory, scientists should be able to develop methods for halting the growth of disease-causing yeast. This research may lead to urgently needed new drugs to improve the treatment of serious yeast infections, which cause much illness and death, especially in patients with compromised immune systems.

Searching for Structures

NIGMS plays a pivotal role in the support of research that determines molecular structures at high resolution. Much of our current understanding of the detailed mechanisms by which biological molecules function has come from studies in this field of structural biology. Among the areas in which impressive progress has been made are the determination of structures of proteins that are known to regulate gene activity and new insights into how proteins fold into their active forms. Since a thorough understanding of a molecule's structure can point to ways to manipulate that structure--either to enhance activity or to change it--these studies have important practical applications in the pharmaceutical and biotechnology industries.

In each of the past several years, significant new findings have been made by teams of scientists supported by NIGMS to apply the techniques of structural biology to the design of drugs for the treatment of AIDS. This year, the team led by Dr. David Matthews of Agouron, a California biotechnology company, determined the three-dimensional structure of RNase H, a protein that is critical to the life cycle of the AIDS virus. Knowledge of this structure could provide a valuable target for the rational design of anti-AIDS drugs.

Biorelated Chemistry

NIGMS also approaches drug design through its substantial support of basic research in chemistry, especially work aimed at the synthesis of natural products. An example of the importance of synthetic chemistry is related to the promising anticancer drug taxol, which, is currently derived from yew trees. Because each yew yields only a small amount of taxol and because the trees are in limited supply, scientists are racing to find ways to synthesize this compound in the laboratory. Many of the techniques that they are using were developed by NIGMS grantees, including Dr. K. Barry Sharpless of MIT and Nobel Prize winner Dr. E.J. Corey of Harvard University. Interestingly, much of the current attention to this drug was stimulated by NIGMS-supported research done in the late 1970's, which showed that taxol works by interfering with the normal breakdown of microtubules. These structures have an important role in cell division, cell movement, and the transport of substances within the cell. Once taxol's mechanism of action was found, its potential use as a cancer chemotherapeutic agent became clear, and the National Cancer Institute has been sponsoring studies using taxol ever since.

New Tools

In the course of conducting their research, NIGMS-supported scientists have developed or contributed to a number of new technologies that play important roles in both basic research and biotechnology. For example, Dr. Francis Barany of Cornell University has devised an important variation on the powerful polymerase chain reaction that improves the detection of small changes in DNA sequences, such as those responsible for many inherited disorders. Although Dr. Barany's technique, called the ligase chain reaction, is still in the early stages of development, it holds great promise for increasing the accuracy of diagnostic tests for a number of diseases.

Another very exciting technology could increase the speed and accuracy--and reduce the cost--of detecting genetic sequences, thus aiding in the diagnosis of genetic diseases. NIGMS grantee Dr. David Ward of Yale University has pioneered this approach to study chromosomes, called high resolution fluorescence in situ hybridization. It uses fluorescent tags to label pieces of DNA, which are then bound to matching pieces of DNA on the chromosomes of a particular cell that is being analyzed. By generating tags having different fluorescent energies and using sophisticated microscopes, cameras, and computer software, Dr. Ward can visualize up to 25 different DNA sequences at one time. In addition to being much more sensitive than older methods, fluorescence in situ hybridization does not require the use of radioactive labels or costly individually prepared antibodies. Using one application, termed chromosome painting, Dr. Ward can detect additions, deletions, duplications, and rearrangements of genetic material, any of which may be associated with genetic diseases or malignancies. Dr. Ward has also used the method to indicate the specific order of a series of genes on a chromosome and to answer basic questions that could not previously have been studied, including the timing of gene duplication and the movement of chromosomes during the cell division cycle.

Research Training

Along with its support of cutting-edge basic research, NIGMS supports research training programs that produce new scientists who are prepared to investigate a variety of biomedical questions. For many years, NIGMS has had multidisciplinary training programs in such areas as genetics, cellular and molecular biology, and the pharmacological sciences. More recently, the Institute has added special training programs in fields that have been shown to have a critical need for highly skilled, creative scientific personnel, including biotechnology and molecular biophysics.

The Institute has two programs designed to rectify the historic underrepresentation of minority groups in biomedical research. One, the Minority Access to Research Careers (MARC) Program, supports research training from the undergraduate level through postdoctoral study. I am pleased that this year, out of the 62 MARC Honors Undergraduate Research Training programs, 15 have added students in the freshman and sophomore years of college, and we anticipate that others will follow.

The other program, the Minority Biomedical Research Support Program, makes research grant awards to scientists at minority institutions. The grants are aimed at strengthening the biomedical research capabilities of these institutions, and have the added benefit of affording students the opportunity to work as part of a research team. Both of these programs have impressive records in producing minority biomedical scientists, and both have been identified as models that other organizations should emulate.

In addition, with the encouragement of the Congress, NIGMS has started a new national program of individual predoctoral fellowships for minority students. One hundred and one such fellowships were awarded at the end of fiscal year 1991 to minority students in graduate schools across the country. We were so pleased with the response to this new program that we have issued another call for applications and, with the cooperation of a number of other NIH components, plan to make further awards this fiscal year.

The Future

As we look to the future, with all the excitement it holds, we also reflect on the past. Later this year, NIGMS will celebrate its 30th anniversary, and its minority biomedical research and training programs will celebrate their 20th anniversaries. We are proud of the many accomplishments we have made possible, and we know that the solid base of knowledge and the highly qualified, highly skilled new scientists we have trained will continue to speed the pace of discoveries in the years ahead.

Mr. Chairman, the FY 1993 budget request for NIGMS is $862,069,000. I would be pleased to answer any questions you might have.

KIRSCHSTEIN, DR. RUTH L.
Director, National Institute of General Medical Sciences

October 12, 1926. Brooklyn, New York

Education: A.B., magna cum laude, Long Island University, 1947. M.D., Tulane University School of Medicine, 1951.

Professional History: 1951-52, Internship, Medicine and Surgery, Kings County Hospital, Brooklyn, N.Y. 1952, Assistant Resident, Pathology, Veterans Administration Hospital, Chamblee, Ga. 1952-54, Resident, Pathology, Providence Hospital, Detroit, Mich. 1954-55, Trainee of National Heart Institute and Instructor in Pathology, Tulane University School of Medicine. 1956-57, Medical Officer, Resident in Pathology, Clinical Pathology, Clinical Center, NIH. 1957-60, Medical Officer, Pathologist, Laboratory of Viral Products, DBS, NIH. 1960-62, Chief, Section of Pathology, Laboratory of Viral Immunology, DBS, NIH. 1962-64, Assistant Chief, Laboratory of Viral Immunology and Chief, Section of Pathology, DBS, NIH. 1965-72, Chief, Laboratory of Pathology, DBS, NIH. 1971-72, Assistant Director, Division of Biologics Standards, NIH. 1972-73, Acting Deputy Director, Bureau of Biologics, FDA. 1973-74, Deputy Associate Commissioner for Science, FDA. 1974-present, Director, National Institute of General Medical Sciences, NIH.

Professional Organizations: American Association of Immunologists; American Association of Pathologists; American Society for Microbiology; Institute of Medicine, National Academy of Sciences.

Committee Memberships: Invited member of World Health Organization Expert Group on International Requirements for Biological Substances; Geneva, Switzerland, 1965 and 1971. Invited consultant to World Health Organization concerning problems related to the use of Poliovirus Vaccine, Live, Oral; Geneva, Switzerland, 1967. Member, Primate Research Centers Advisory Committee, Division of Research Resources, NIH, 1971-1975. Chair, NIH Grants Peer Review Study Team, 1975-1976. Chair, PHS Genetics Coordinating Committee, 1976-1979. Member, Fogarty International Center Scholars-in-Residence Advisory Committee, 1977-1982. Member, NIH Coordinating Committee on Manpower, 1978-1983. Chair, PHS Task Force on Women's Health Issues, 1983-1984. Chair, PHS Coordinating Committee on Women's Health Issues, 1984-1990. Co-chair, PHS Coordinating Committee on Women's Health Issues, 1990-present. Member, NIH Advisory Committee for the IOM Study of the Organizational Structure of the NIH, 1983-1984. Member, NIH Peer Review Committee, 1987-1988. Member, HHS Executive Development Board, 1985-present. Member, Federal Task Force on Women, Minorities and the Handicapped in Science and Technology, 1987-1990. Chair, NIH Working Group on Minorities in Biomedical Research, 1988-present.

Honors, Awards: Elected to Institute of Medicine, National Academy of Sciences, 1982. Doctor of Science, Honoris Causa, The Mount Sinai School of Medicine, 1984. Honorary Doctor of Laws, Atlanta University, 1985. DHEW Superior Service Award, 1971. PHS Superior Service Award, 1978. Presidential Meritorious Executive Rank Award, 1980. PHS Equal Opportunity Achievement Award, 1983. Presidential Distinguished Executive Rank Award, 1985. Dr. Nathan Davis Award, American Medical Association, 1990, Honorary Doctor of Humane Letters, Long Island University, 1991.

NIH STRATEGIC PLAN

Mr. NATCHER. Thank you, Dr. Kirschstein.

Now, how does your Institute's basic science mission fit into the draft NIH strategic plan?

Dr. KIRSCHSTEIN. Mr. Chairman, the basic thrusts of the draft strategic plan are very well integrated with the mission of NIGMS.

There has been an emphasis in the framework for the strategic plan on molecular medicine. The NIGMS programs in molecular genetics and cellular and molecular biology are clearly part of that.

There also is an emphasis in the draft plan on structural biology. I just told you about the importance of NIGMS-supported research on three-dimensional structures—or structural biology.

There is also specific emphasis on biotechnology in the proposed plan. NIGMS is the lead Institute in biotechnology and we were charged with preparing the draft section of the strategic plan related to biotechnology.

Mr. NATCHER. Do you see the strategic plan changing the way you do business?

Dr. KIRSCHSTEIN. No, Mr. Chairman. I think the strategic plan is emphasizing the areas of fundamental cross-cutting science that are important to all the Institutes but that have very specific relevance for an Institute like NIGMS, whose mission is to provide the fundamental research which will be important for all the categorical Institutes as they support research in clinical areas.

BIOPHYSICS PROGRAM

Mr. NATCHER. In your budget, the biophysics area receives the largest increase. Would you say this is your top priority science area?

Dr. KIRSCHSTEIN. Mr. Chairman, it is certainly among the top priority science areas. As I said before, the area of structural biology, which is biophysics basically, has come to fruition in the last few years; and we feel this is an enormously important area to emphasize, not only to generate the information that will be important for research in many other areas, but also for many industries, which are now trying to use three-dimensional structures to design drugs and antiviral agents and—perhaps even vaccines—using approaches based on rational drug design. However, scientific areas like pharmacology, genetics, and cell biology are also extremely important.

COST MANAGEMENT

Mr. NATCHER. How is your Institute handling the downward adjustment of grant awards in 1992 and 1993?

Dr. KIRSCHSTEIN. Mr. Chairman, although the individual who receives a grant award, which is not in the amount that was recommended by the study section, cannot help but feel that this constitutes downward negotiation. In fact, we are not continuing across-the-board downward negotiations.

We are meeting previous commitments. One of the most important things that cost management has permitted us to do is to set the level of each year of the grant when we make the first year of the award. This means that scientists can predict, for the future years of that grant award, what their level of support will be. However, in order to provide for a reasonable number of research grants, we analyze each grant application individually, and examine the budget of each individually after obtaining the study section recommendations and the advice of the National Advisory General Medical Sciences Council. Members of the staff analyze this information and determine an appropriate level of support.

This does, in fact, mean that there are some reductions from the level recommended by the study section. In 1992, the reduction will be 12.5 percent, on average; in 1993, we are predicting a 15.6 percent reduction. However, on average, those grants for continuing competing awards are being increased, by the biomedical R&D price index level of about 5.1 percent, above the previous level.

Mr. NATCHER. You have expressed concern about limiting funding increases for competing renewal grants. Should a renewal need to be increased by 10 percent or more if it is an extension of an earlier project?

Dr. KIRSCHSTEIN. Mr. Chairman, that would vary from grant situation to grant situation. The concern we have had, and still have, is for the young investigator. When such a young investigator has just gotten his or her first research results, the time for expansion is at the first renewal.

We have had some concerns about whether such a person will be able to receive funds sufficient to mount the appropriate expansion. However, in order to garner funds for a sufficient number of investigators, all of whom are doing absolutely superb work, we realize that sometimes providing that expansion of funds may not be possible.

Mr. NATCHER. In 1991, many of your grants were approved for five years of support, but given four-year awards. Are you satisfied, Doctor, with the four-year average grant limit in the financial management plan?

Dr. KIRSCHSTEIN. In general, I think we are satisfied, Mr. Chairman. There have been advantages to providing investigators, particularly new ones, with a longer grant period. However, as that began to occur, commitments to fund those longer grants would have resulted in the institute being able to support fewer of the superb competing applications that we received; so we felt that moving back to a four-year grant period might be appropriate.

Mr. NATCHER. For several years you have considered a researcher's other sources of funding when awarding grants. How has the outside research community reacted to this policy, Doctor?

Dr. KIRSCHSTEIN. In general, Mr. Chairman, in discussions we have had both with members of the National Advisory General Medical Sciences Council and with scientists across the country, there has been an understanding of what we are trying to do.

The reason for considering the total support of an investigator is to try to provide the means to continue the research career of the new investigator, the investigator who has no other means of support, and who is just on the wrong side, if you will, of the funding cutoff. In fact, the NIGMS posture in this regard has some similarities to what Dr. Healy was trying to do in establishing the Shannon Award.

There are, of course, some funded investigators, who, if their support is limited, are not going to be very happy. However, the National Advisory General Medical Sciences Council discusses those investigators' applications individually, and if they are very outstanding, and are doing essential and really "earth-shaking" research, we usually allow the projects to continue to receive Institute funds.

GENBANK

Mr. NATCHER. Why are you transferring the GENBANK to the National Library of Medicine?

Dr. KIRSCHSTEIN. The National Institute of General Medical Sciences has, over the the years, as part of its mission of trying to provide needed research resources to the scientific community, evaluated a number of needs. About 10 years ago, it was felt that a nucleic acid genetic sequence data bank was needed to gather and distribute sequence information that would allow grantees to make progress that they could not make otherwise. NIGMS took the lead and established that nucleic acid genetic sequence data bank, GENBANK. Several years ago, the National Library of Medicine established a new unit, the National Center for Biotechnology Information.

In recent discussions at the NIH level and with Dr. Lindberg, the Director of the National Library of Medicine, it was decided that this data bank would be more appropriately housed within the National Library of Medicine, which compiles and distributes a great deal of other medical and scientific data.

BUDGET LEVELS FOR MINORITY PROGRAMS

Mr. NATCHER. Your Institute's budget increases by 5.8 percent, which is higher than the NIH average. Doctor, why didn't you use any of this increase for your minority programs?

Dr. KIRSCHSTEIN. Mr. Chairman, there are two minority programs that NIGMS supports. One is the Minority Access to Research Careers Program, which is a research training program and is authorized under the National Research Service Act.

As you know, authorization for that legislation has not been renewed, and therefore, the Congress did not allocate extra funds for that program. We regret that greatly, because some of our activities and some of the new initiatives that we want to undertake cannot be as well supported.

In addition, in the requirements as to how NIGMS was to formulate the 1993 budget, the only area that was allowed to increase was the research project grant line. All other mechanisms, including the category of "other research", which includes the Minority Biomedical Research Support Program, were essentially straightlined. We regret that very much, because we feel very keenly that increasing our minority programs is among our highest priorities and may indeed, even be our highest priority.

Mr. NATCHER. Mr. Stokes, I yield to you.

MINORITY OPPORTUNITIES IN RESEARCH PROGRAMS BRANCH

Mr. STOKES. Thank you, Mr. Chairman.

Dr. Kirschstein, it is always a pleasure to welcome you before the Committee. Let me begin by asking you about the MORE programs.

In 1991, NIGMS established the MORE Programs Branch to serve as the administrative umbrella for MARC and MBRS. I spoke with you last year about the diminishment of these programs. Where are we?

Dr. KIRSCHSTEIN. The administrative structure for the Minority Opportunities in Research Programs Branch has been established. The MARC Program, the MBRS Program, and a group of new special initiatives, such as the individual predoctoral fellowships, and some special initiatives which NIGMS will mount in cooperation with the Office of Minority Programs, will all be distinct units within the MORE Programs Branch.

As you know, we will not diminish in any way—in fact, we hope to enhance them—the budgets and activities of MARC and MBRS. In the budget, the MBRS Program budget and the MARC Program budgets are presented separately as sub-units of the MORE Program, and they will be presented in that fashion in the future, as well.

Mr. STOKES. Have you set up a separate office?

Dr. KIRSCHSTEIN. We are in the process of doing that. The office will be similar to those of my other programs. The director of the MORE Program will oversee the activities of the MARC and MBRS Programs and will work collaboratively with the directors of those two programs and with me. There will be no diminishment of what is going on in those programs.

Mr. STOKES. Where are we in terms of a director for that?

Dr. KIRSCHSTEIN. We hope to be able to start recruiting in the very near future.

Mr. STOKES. Can you be more specific with reference to the time frame?

Dr. KIRSCHSTEIN. I would hope that we would have somebody by late summer or early fall.

MARC AND MBRS PROGRAMS

Mr. STOKES. Can you give us some idea of what programmatic or directional changes you envision in the foreseeable future relative to MARC and MBRS programs?

Dr. KIRSCHSTEIN. First of all, Mr. Stokes, I think both of the programs are functioning well, and doing the jobs that they were established to do. We are concerned that, without sufficient funds, we will not be able to expand some of their activities.

We have been concerned for some time that some of the institutions that had MBRS awards in the past have lost those awards during the peer review process. Because of that, and as you requested, we have begun a process to try to help those institutions to regain such awards. We have planned a series of workshops at which staff from NIGMS would meet with the faculty and administrators of many of those schools, particularly HBCUs, in order to provide them not only with an overall picture of what is required in an application, but to talk with them individually in small, one-on-one sessions or small individual sessions about their unique concerns.

We held the first one of those workshops in Charlotte, North Carolina, in the second week of February. We have three or four more planned.

Unfortunately, as a result of serious travel fund restrictions, we will not be able, within fiscal year 1992, to hold any more of those workshops, but we plan to hold them as soon as we can in fiscal year 1993.

FY 93 REQUEST FOR MINORITY PROGRAMS

Mr. STOKES. Dr. Kirschstein, for fiscal year 1993, $47,700,000 has been requested for MARC, MBRS, and the other special initiatives. Last year, you indicated that despite the creation of the umbrella category, NIGMS would present them individually in the budget to Congress. All these programs were level-funded, however, for the fiscal year 1993.

What level of funding is proposed for MARC in fiscal year 1993?

Dr. KIRSCHSTEIN. $13,220,000.

Mr. STOKES. Is that the same as last year's level?

Dr. KIRSCHSTEIN. Yes, sir.

Mr. NATCHER. What level for MBRS for fiscal year 1993?

Dr. KIRSCHSTEIN. $33,059,000 in NIGMS funding. There are, in addition, as you know, MBRS funds from other Institutes as line items in their proposed budgets. Those amount to $12,600,000, bringing the total to about $45,900,000.

Mr. STOKES. So, that takes it above the other funding of $33,100,000?

Dr. KIRSCHSTEIN. Yes, although the funding from other Institutes remains at the 1992 level as well.

SPECIAL MINORITY INITIATIVES

Mr. STOKES. What level will be provided for the other special initiatives?

Dr. KIRSCHSTEIN. The same as last year's, $1,300,000.

Mr. STOKES. Is there a reason why there is no increase in any of these areas with the one exception?

Dr. KIRSCHSTEIN. The budget parameters within which we were working required that all mechanisms, other than research project grants, be straight lined from 1992. However, Mr. Stokes, there are some new initiatives which NIGMS will be able to undertake in 1993 because the Office of Minority Programs—which does have, I believe, about $10,000,000 for various minority activities including training—has asked NIGMS to undertake two new initiatives. These are what are called "bridging programs."

Dr. Ruffin agreed that we could present these to you. He will be here, as you know, on Thursday, March 26. Since we are working in collaboration with him, and since we are presenting first, he agreed we could talk to you about these.

In 1992, there will be $2,000,000 added to the NIGMS minority activities budget with which we will begin funding for two bridging programs. The first is a program for minority students in either two-year minority schools or two-year schools or junior colleges which have substantial numbers of minorities. The program will be designed to allow those students to move easily into science baccalaureate programs at four-year colleges.

We know from data from various studies that one of the weak points in the college careers of some minority students is at the end of the second year. More of those students, who are either attending junior colleges or even four-year colleges, drop out at the end of the second year; and unfortunately, then they may be lost. So we are very anxious, and Dr. Ruffin is also, to design a program that will give those students support and allow them to move on to a four-year college.

The second bridging program is for graduate students from universities which confer the Master's degree in Science, as the terminal degree. We think it is very important for young, budding scientists to go on to get the doctoral degree. So that is a second bridging program, allowing students to move automatically from a school where they can only obtain a Master's degree to a doctoral degree program.

We are accepting applications for those two programs now. We hope to make somewhere between six and ten awards before the end of the fiscal year for $2,000,000.

Mr. Stokes. Then, I gather from what you are telling me that, in the absence of Dr. Ruffin and the Office of Minority Health providing this bridging funding, you would not be able to do what you are telling us that you are going to do?

Dr. Kirschstein. We would not be able to. These were programs we had talked about for many years. Dr. Ruffin, before he came to NIH, and I had talked about such programs. He was, as you probably know, a member of our MARC review committee, so I have known him for many years.

These were initiatives we really wanted to do and have not been able to do. We are pleased that some funds have been allocated to Dr. Ruffin's office, and he is willing to give us some of the money in order to work with him on these bridging programs. But, unfortunately, if he had not come to the rescue, we would not have been able to mount these programs.

IMPACT OF LEVEL FUNDING

Mr. Stokes. How has this level funding affected the grants or the students participating in the programs?

Dr. Kirschstein. It is a serious problem. The number of students, the level, remains the same. But, for example, level-funding will affect the MARC program—where we have started, with your encouragement, a freshman and sophomore portion of the Honors Undergraduate Research Training Program. As renewal applications come in with requests for support for first- and second-year students, as well as third- and fourth-year students, we will now have to assess how to distribute the same number of student slots over all four years. We are not at all pleased about that.

Mr. Stokes. Needless to say, neither am I, because as we have gone along over the years, we have discussed the absolute necessity for this type of program; and even in spite of the program, we are still way behind in terms of where minorities ought to be in the field of science.

Dr. KIRSCHSTEIN. Absolutely.

FUNDING REQUESTS FOR MINORITY PROGRAMS

Mr. STOKES. What level of funding did NIGMS recommend to the Department for this program?

Dr. KIRSCHSTEIN. For MBRS, we requested $40,400,000; for the MARC program, we requested $19,800,000; and for special new initiatives, which includes the individual fellowship program, we requested $5,700,000. That is a total of almost $66,000,000.

Mr. STOKES. The amount that is in your budget, is this the amount that OMB approved?

Dr. KIRSCHSTEIN. Yes, the $47,671,000 is the amount that OMB approved, yes, sir.

Mr. Stokes, I might add that NIGMS has shown its commitment in other ways, as well. As you know, NIH has a program of administrative supplements for minority investigators, graduate students, postdoctoral students, college students and sometimes even high school students, who can be added to the budget of a research grant to obtain training, or to retool or establish collaborations in the case of investigators. Over recent years, this has been very successful.

It is a program that the Institute can easily administer. Any investigator holding an NIGMS research grant simply has to request the Institute to add such a minority scientist or aspiring scientist. In 1992, NIGMS allocated $3,800,000 of its research project grant funds for those administrative supplements, and we propose to use $4,100,000 for those supplements in 1993.

Mr. STOKES. I appreciate that. Thank you.

Thank you, Mr. Chairman.

DEPARTMENT OF EDUCATION POLICY ON MINORITY SCHOLARSHIPS

Mr. NATCHER. Now, Dr. Kirschstein, does the new education department policy on scholarships targeted to minorities, have any impact on your minority training programs?

Dr. KIRSCHSTEIN. Mr. Natcher, we are concerned about that. We do not know for sure whether that will have an impact or not on the Institute programs. We are particularly concerned about it with regard to the individual fellowship programs and these administrative supplements that I have just been describing.

The MBRS Program, and the MARC Honor Undergraduate Research Training Programs, make awards to institutions that have substantial enrollments of minority students. The Department of Education has stated that institutional awards are appropriate.

For the individual fellowships and these administrative supplements, we do have some concerns. However, we understand that the proposed rule from the Department of Education states that if programs are Congressionally mandated, they would be exempt; and since the funds for the special initiatives and for some other activities have been specially provided by the Appropriations Committee and, therefore, by the Congress, we hope that these would be exempt.

RESEARCH TRAINING STIPENDS

Mr. NATCHER. Under the President's budget, there would not be an increase in research training stipends for two years. Should you consider decreasing the number of trainees in order to provide stipend increases?

Dr. KIRSCHSTEIN. We are deeply concerned about the level of stipends that NIH can pay to trainees. In the case of NIGMS, this especially impacts the predoctoral, the pre–Ph.D. student.

Our stipend for them is $8,800. That compares to a stipend from the National Science Foundation of $14,000. We recently heard that NASA and, in some cases, the Department of Energy pays a stipend of $16,000.

On the other hand, because of increased costs in other parts of the training grant budget, particularly, the increase in tuition, we have had concerns about limiting stipend levels to preserve the number of students that we can support. So it is a delicate balance.

Overall, we are deeply concerned and feel that stipends do need to go up.

RESEARCH TRAINING GRANTS

Mr. NATCHER. Are you comfortable with your Institute's mix of institutional and individual training grants?

Dr. KIRSCHSTEIN. Yes, sir.

Mr. NATCHER. How many trainees do your combined M.D. and Ph.D. programs support and how does this compare to your target for other programs?

Dr. KIRSCHSTEIN. We support in 1992, and will be proposing to support in fiscal year 1993, 783 such trainees. We would feel that the appropriate level would be 875.

Mr. NATCHER. How many biotechnology trainees are funded in your 1993 request?

Dr. KIRSCHSTEIN. There are 305.

Mr. NATCHER. How does that compare to the number suggested in your five-year plan, Doctor?

Dr. KIRSCHSTEIN. It is woefully behind what was suggested in the five-year plan. That number of biotechnology trainees that should be supported was estimated to be 1,500 by 1993.

Mr. NATCHER. Your budget documents indicate that you are considering a new joint training program in chemistry and biology. Would you begin this program even if no new funding were available and you had to reallocate training dollars, Doctor?

Dr. KIRSCHSTEIN. Mr. Natcher, we feel that it is a very important area. We think that it is an area related to the continued success of the biotechnology and pharmaceutical industries. We are trying to make some plans and have talked about the possibility of working with industries, perhaps, for example, pharmaceutical houses, in some sort of a collaborative venture to support such a program.

We are just beginning this planning process. We have made a modest announcement to see what the degree of interest is and what we might do. We hope we can work collaboratively with industry and develop a program which could be started very slowly even without new funds.

Mr. NATCHER. What steps, Doctor, are you taking to make research training dollars go further, such as limiting reimbursements for tuition increases?

Dr. KIRSCHSTEIN. NIGMS for years has been concerned about limiting reimbursement for tuition and has taken the lead in implementing such proposals. Now NIH as a whole now has agreed to do this. We are currently surveying the tuition levels at participating institutions. We anticipate that there will be some sort of an upper limit put on tuition reimbursements during this fiscal year.

We think this is a very important phenomenon. As you know, tuition has recently been increasing at the rate of 10 percent a year. When one pays full, increasing tuition, that erodes the number of trainees who can be supported.

CHARACTERISTICS OF BASIC RESEARCH GRANTS

Mr. NATCHER. Are there any notable differences between grantees who do basic rather than disease-specific research, for example, Doctor, in their age, success rate, or size of grant?

Dr. KIRSCHSTEIN. The size of grant for a researcher who is doing fundamental, undifferentiated research is generally somewhat lower than the size of a grant for clinical research.

One of the notable differences is that, whereas the Institutes that are concentrating on disease-related research provide about 90 percent of their funds primarily to medical schools, the National Institute of General Medical Sciences only provides about 50 percent of its funds to medical schools and the other 50 percent goes to colleges and universities throughout the country—often to state universities and to small colleges. For example, we are the major supporter of the small college program, known as the Academic Research Enhancement Awards (AREA) program.

USE OF FUNDS TRANSFERRED FROM NCI

Mr. NATCHER. How do you plan to use the $1,500,000 transferred this year from the Cancer Institute?

Dr. KIRSCHSTEIN. Mr. Chairman, we were very pleased that Dr. Healy provided NIGMS with about $1,500,000 in cancer funds because the researchers supported by NIGMS are doing fundamental research that is very important to cancer. For example, the entire recombinant DNA field, which was developed and supported by NIGMS, is essentially what led to the discovery of oncogenes.

Basically, those funds will support research in cell growth. The study of proteins, like cyclins, which regulate the growth of cells and whose function goes awry in the proliferation of cells which are malignant, is very important. We will use these funds for research grants directly related to such areas.

Mr. NATCHER. Is this funding included in your 1993 base?

Dr. KIRSCHSTEIN. Yes, sir.

Mr. NATCHER. Mr. Stokes.

FRESHMAN-SOPHOMORE EXPANSION OF MARC PROGRAM

Mr. Stokes. Regarding the inclusion of freshmen and sophomores in the program, how many are included?

Dr. Kirschstein. Sixty-three.

Mr. Stokes. Has the inclusion been a good idea?

Dr. Kirschstein. Yes. We first started the freshman and sophomore program by requesting that ongoing MARC grants submit supplemental requests. Supplemental awards are supporting those 63.

We are now asking that, as the MARC training grants come up for renewal, applications propose the inclusion of the freshman-sophomore component if they wish to, and we think many will.

NATIONAL PREDOCTORAL FELLOWSHIPS FOR MINORITIES

Mr. Stokes. Regarding the predoctoral fellowship program, last year, you indicated you wanted to expand eligibility in this program. What action has been taken in reference to this activity?

Dr. Kirschstein. As you know, we put out an announcement in FY 1991 saying that we would award funds which this committee specially appropriated for fellowships for minority students enrolled in graduate schools throughout the country. One goal of initiating these fellowships was to ensure that students supported under the Minority Biomedical Research Support Program would be eligible, since eligibility for the original predoctoral fellowship program we had had was confined to students who were graduates of the Honors Undergraduate component of the MARC program.

The announcement was made in 1991 and we received about 150 outstanding applications. We anticipated making awards for 65 to 70 fellowships. There were so many good applications that we made 101 awards; 65 were made using the funds NIGMS had, and the remainder were supported by a number of other Institutes. The Office of Minority Programs also provided funds for some of those.

Mr. Stokes. So, what level of funding was provided for fiscal year 1992 and what are you recommending?

Dr. Kirschstein. It was $1,400,000.

Mr. Stokes. For 1993?

Dr. Kirschstein. It will be the same.

We, however, are so excited about this program that we have reannounced it, in cooperation with several other Institutes, and we are determined to find funds to make about 45 additional awards in FY 1992.

Mr. Stokes. To what extent do MBRS students participate?

Dr. Kirschstein. They are eligible. Ten of the fellowships were given to student participants in the MBRS Program, four of whom are attending Meharry Medical College.

MINORITY BIOMEDICAL RESEARCH SUPPORT PROGRAM

Mr. Stokes. You have now had MBRS under your jurisdiction for——

Dr. Kirschstein. About two-and-a-half years, sir.

Mr. Stokes. This program is not up for reauthorization, is it?

Dr. Kirschstein. No. This program does not require reauthorization similar to the MARC program, which is authorized under the NRSA.

Mr. Stokes. Is an increase permissible for fiscal year 1993 for this program?

Dr. Kirschstein. Yes.

Mr. Stokes. What level of funding was requested by NIGMS?

Dr. Kirschstein. $40,500,000.

Mr. Stokes. And the level approved by OMB?

Dr. Kirschstein. $33,059,000.

Mr. Stokes. How many students and institutions are involved in this program?

Dr. Kirschstein. There are 96 institutions and about 1,400 students. The number of students involved varies because these students are not being supported for training but rather as research assistants or research associates. They are employees of the institution, and their numbers vary a little from year to year. It is about 1,400 now.

Mr. Stokes. Obviously, this is an area where additional funding would enable you to do a much better job?

Dr. Kirschstein. Yes, sir.

MINORITY PROGRAMS SYMPOSIUM AND WORKSHOPS

Mr. Stokes. I understand the NIGMS held a minority program symposium in November. Your justification indicates other regional meetings are planned. Where in the process is the Institute in convening these workshops?

Dr. Kirschstein. First of all, the Minority Programs Symposium is an event to which we bring as many of the students as is possible from all the schools supported by both MARC and MBRS. There are 44 of the 96 MBRS institutions that also have MARC programs, and then another almost 20 institutions that have MARC that do not have MBRS. We bring these students and institutional representatives together for a symposium once every year or two.

We were delighted that you came last November and gave the keynote address at the symposium. It was greatly appreciated.

In addition to that symposium, we have planned some regional workshops. The first was held in Charlotte, N.C., in February. These workshops are designed specifically to try to get minority institutions that have never participated in MARC or MBRS or who have participated and, for one reason or another, are not funded at the present time, to be able to submit competitive grant applications for one or the other program, or both programs.

At that first regional workshop in Charlotte, 22 institutions, out of 25 that we contacted, attended. It was an extremely successful workshop. We hope we will get applications from them.

We have planned three or four more of those workshops across the country, but unfortunately, we will not be able to hold them in fiscal year 1992 because we do not have the travel funds for our staff to attend. Those workshops clearly need our staff input or they will not be successful.

Mr. Stokes. You are referring, of course, to the cuts in travel expenses last year.

Dr. KIRSCHSTEIN. Yes, sir.

PARTICIPATION IN MARC AND MBRS PROGRAMS

Mr. STOKES. We recognize that this has been a problem for all of our agencies in seriously impeding their ability to carry out their functions.

Has the Institute noted any increase in the number of institutions seeking eligibility in the MARC and MBRS programs?

Dr. KIRSCHSTEIN. We have had new applications from several schools. In some cases, if a currently supported or a previously supported school does not fare well when its application for support is reviewed, we have been able to start a few new MARC programs. Basically, we have not been able to do as much of that in the MBRS program, but we did start a program at the University of Guam.

Mr. STOKES. I would appreciate it if, for the record, you would tell us in each category what number serve Native American, Hispanic, and black populations; and also provide a three-year comparison for us.

Dr. KIRSCHSTEIN. We will do that.

[The information follows:]

Participation by Category of Institutions in the MARC and MBRS Programs

Primary Minority Population Served:	FY 1989 Number of Institutions MARC	FY 1989 Number of Institutions MBRS
Black Americans	38	50
American Indians	3	5
Hispanic Americans	6	13
Puerto Ricans	3	8
Asian/Pacific Islanders	1	2
Mixed Population	11	12
Total Institutions	62	90

Primary Minority Population Served:	FY 1990 Number of Institutions MARC	FY 1990 Number of Institutions MBRS
Black Americans	37	56
American Indians	3	5
Hispanic Americans	6	11
Puerto Ricans	3	9
Asian/Pacific Islanders	1	2
Mixed Population	11	15
Total Institutions	61	98

Primary Minority Population Served:	FY 1991 Number of Institutions MARC	FY 1991 Number of Institutions MBRS
Black Americans	38	53
American Indians	4	5
Hispanic Americans	7	11
Puerto Ricans	4	8
Asian/Pacific Islanders	1	3
Mixed Population	9	16
Total Institutions	63	96

Mr. STOKES. Lastly, let me just say, Dr. Kirschstein, you mentioned earlier that you have been director out there for 18 or 19 years. For a large part of that time, I have had the pleasure and privilege of working with you across this table and also through my office and your office.

I just want to say, I appreciate very much the dedication and commitment you have put into these programs. Hopefully, some day you will have the money to go with the commitment to really make things happen.

Dr. KIRSCHSTEIN. Mr. Stokes, that is my fondest dream also.

Mr. STOKES. Thank you very much.

Thank you, Mr. Chairman.

Mr. NATCHER. Dr. Kirschstein, we want to thank you and your associates for appearing before our Committee on behalf of your budget request for fiscal year 1993. It has been a good hearing, Dr. Kirschstein, just like it always is. Thank you.

We will reconvene at 2:00 o'clock.

[The following questions were submitted to be answered for the record:]

MINORITY TRAINING ACTIVITIES

Mr. Natcher: How does the $25 million proposed in the Office of the Director for minority training activities relate to your training programs?

Dr. Kirschstein: Dr. John Ruffin, Director of the Office of Minority Programs in the Office of the Director, NIH, has begun to formulate plans for the allocation of funds provided to his office for minority training activities. Those plans include the funding of two initiatives which NIGMS will administer: one which will support programs to facilitate the transition of minority students from two-year colleges to institutions awarding the baccalaureate degree in the sciences, and the other which will fund programs to facilitate the transition of students from Master of Science degree programs to Ph.D. programs. These have been identified as critical points in the progression of underrepresented minorities through educational experiences to research careers. These initiatives, and others which are being planned, are likely to complement the efforts of the Institute's own programs aimed at increasing the participation of minorities in biomedical research, since they will largely address heretofore unaddressed parts of the educational and career pipeline.

MINORITY BIOMEDICAL RESEARCH SUPPORT

Mr. Natcher: Identify the 1992 and 1993 funding for the MBRS program from all sources, including ADAMHA.

Dr. Kirschstein: The following table lists the NIGMS contribution as well as the cofunding amounts budgeted for MBRS by other components of NIH, or contributed by the National Institute of Alcohol Abuse and Alcoholism, ADAMHA, for both FY 1992 and FY 1993.

MINORITY BIOMEDICAL SUPPORT PROGRAM
(Dollars in Thousands)

	FY 1992	FY 1993
NIGMS	$33,059	$33,059
NCI	3,064	3,064
NHLBI	2,672	2,672
NIDR	177	177
NIDDK	1,672	1,672
NINDS	219	219
NIAID	798	798
NICHD	566	566
NEI	335	335
NIEHS	462	462
NIA	1,389	1,389
NIAMS	420	420
NIDCD	493	493
NCRR	358	358
NIAAA	235	235
SUBTOTAL COFUNDING	12,860	12,860
TOTAL MBRS FUNDING	$45,919	$45,919

NEW HIRE

Mr. Natcher: What position will the new health science administrator requested in your RMS budget hold?

Dr. Kirschstein: We anticipate hiring a health scientist administrator to manage a portfolio of grants in the Genetics Program.

STIPEND LEVELS

Mr. Natcher: Identify the range of pre- and postdoctoral stipends paid from NIH research training grants.

Dr. Kirschstein: All predoctoral students on National Research Service Award (NRSA) institutional training grants receive a stipend of $8,800 per year. The levels of NRSA postdoctoral trainee stipends are dependant on the years of relevant experience each trainee possesses at the time of appointment and are as follows:

Experience	Stipend
0 years	$18,600
1 year	19,700
2 years	25,600
3 years	26,900
4 years	28,200
5 years	29,500
6 years	30,800
7 years	32,300

Freshmen/sophmore students supported by the MARC Honors Undergraduate Research Training (HURT) Program receive $4,800 in stipend support, while Juniors/Seniors receive $6,732.

COMPONENTS OF THE MINORITY BIOMEDICAL RESEARCH SUPPORT PROGRAM

Mr. Natcher: What is the allocation of MBRS funding between the Traditional Program and the Undergraduate College Program?

Dr. Kirschstein: In FY 1991, the traditional MBRS program, including co-funding, received $40.8 million or approximately 96 percent of the total MBRS funding. The Undergraduate College Program received $1.8 million or approximately 4 percent of the total MBRS funding.

MINORITY ACCESS TO RESEARCH CAREERS PROGRAM TRAINEES

Mr. Natcher: Identify the number of trainees supported under the MARC Program for 1991-1993.

Dr. Kirschstein: The number of trainees supported under the MARC program is provided in the following table:

MARC FULL-TIME TRAINING POSITIONS

	FY 1991	FY 1992	FY 1993
INDIVIDUAL			
Predoctoral Fellowships	73	77	77
Faculty Fellowships	7	3	3
Subtotal Individual	80	80	80
INSTITUTIONAL			
Undergraduate	559	559	559
Postdoctoral	4	4	4
Subtotal Institutional	563	563	563
TOTAL, MARC	643	643	643

MEDICAL SCIENTIST TRAINING PROGRAM

Mr. Stokes: NIGMS administers the Medical Scientist Training Program, a program that is productive and unique among the training programs of the NIH.

For the record, would you provide the number of MSTP programs, the number of trainee slots supported by the program and a list, by name and institution, of underrepresented minorities that have been supported by the program within the last five years?

Dr. Kirschstein: The number of MSTP programs and the number of trainee slots supported by the program for the last five years is given below:

FISCAL YEAR	NUMBER OF PROGRAMS	NUMBER OF TRAINEES
1987	28	719
1988	29	728
1989	29	735
1990	29	766
1991	29	783

The information you requested regarding the number of underrepresented minorities supported by the various institutions has not been a reporting requirement for the recipients of MSTP awards, or for any other training grants, since we were not permitted to collect such data. However, in informal discussions with MSTP Program Directors in FY 1989, approximately 4 percent of the trainees supported by the grants were identified as underrepresented minorities. This ratio increases to 6 percent when the total enrollment of trainees at these institutional programs, i.e., those supported by non-MSTP funds, are included.

In FY 1991, the NIH revised the Statement of Appointment form that is submitted for all trainees funded on NRSA institutional training grants, including MSTP grants. The form now requests that race/ethnicity for each student be voluntarily provided. Since the reporting of race/ethnicity is voluntary, and this effort was just initiated, it is too early to predict how helpful the revised requirement will be in terms of collecting and monitoring an institutions' commitment to minority recruitment. The success of MSTP training grant recipient institutions in recruiting minorities into their programs will be assessed as part of peer review when those institutions submit applications for renewal grant support.

Mr. Stokes: MSTP is in its 20th year of operation, and has not been evaluated. Are there any plans to evaluate this program? Why or why not?

Dr. Kirschstein: At least two evaluations of the MSTP have been conducted in the past by NIGMS staff, and the NIGMS recently awarded a contract to support the services of professionals with expertise in the evaluation of research training programs to begin planning a new study. This initial planning phase will be completed over the coming two to three months, at which time the NIGMS will begin the formal study design process.

Previous evaluations conducted in 1979 and 1984 included the collection of data on educational and career outcomes of former trainees, and on several measures of research activity, such as having NIGMS and NSF grant support and publishing research results. In addition, several of the 29 NIGMS funded MSTP programs have conducted and published the results of evaluations of their own graduates. In the latest study that NIGMS performed, 67 percent of former MSTP trainees had received the M.D.-Ph.D. degree. Of these, 55 percent were in postdoctoral training and 45 percent had entered their professional careers. Of this latter group, 88 percent were in academic and research positions. In addition, we also have evidence based on the various honors, such as the Lasker and the Passano Awards bestowed on graduates of the MST Program, that these students truly are outstanding.

SMALLER INSTITUTIONS

Mr. Stokes: Many of our smaller, liberal arts, and two-year institutions serve a significant minority student population. The economics and regulations associated with high tech research are becoming prohibitive at some of these small schools.

What efforts are underway to retain and expand the participation of these small institutions within the programs of NIGMS?

Dr. Kirschstein: The Minority Biomedical Research Support (MBRS) Program has several components, one of which is specially designed for the types of institutions that you singled out. The MBRS Program for Undergraduate Colleges supports enrichment activities for both faculty and students, as well as pilot and regular research projects for faculty. The enrichment activities often include summer or school term research experiences at off-campus laboratories so that faculty can enhance their research skills. The goal of all of these experiences is to improve the research capacity of the faculty and institution. Some institutions find that this grant mechanism suits their situations best. Other small, liberal arts colleges, in particular, take advantage of still other grant mechanisms. Many participate in the other components of the MBRS Program, which fund faculty and/or student research experiences. In addition, NIGMS tries to encourage and provide helpful advice to institutions which are eligible to apply for the Academic Research Enhancement Award Program. This program supports feasibility studies and other small scale research projects by faculty at undergraduate institutions that are not "research intensive." The agenda for the series of regional workshops that NIGMS has initiated stresses all of these mechanisms of research enhancement and support, since individual institutions may find one better suited to their interests and capabilities than others.

PROMOTION OF MINORITIES

Mr. Stokes: Dr. Kirschstein, you have been the Director of the NIGMS for some 18 or 19 years, I believe. You have contributed significantly to enhanced participation of minorities and women in the area of biomedical research during your tenure. How many minorities within your institute have been promoted to the ES or SES levels?

Dr. Kirschstein: The Institute currently has six SES positions, four of which are occupied by women, two by males. It is important to note that all six of these positions have been filled for approximately two or more years. The last SES vacancy filled was that of Deputy Director, NIGMS. Prior to Dr. Marvin Cassman's appointment, Dr. Luther Williams, a distinguished African American scientist and administrator, served as Deputy Director.
Dr. Williams left the NIGMS to accept an SES equivalent position with the National Science Foundation.

Mr. Stokes: What efforts are you taking to promote minorities within NIGMS?

Dr. Kirschstein: NIGMS has been quite successful in its efforts to recruit and retain well-qualified minorities, as evidenced by the fact that approximately 58, or 28 percent of the Institute's staff, are members of underrepresented minorities. Of these employees, 43 have already been promoted to the top of their career ladder. Of the remaining 15, nine were promoted in the last 12 months, and five have been with the Institute for less than one year, thus are not eligible for promotion.

We also routinely establish trainee positions within the Institute for professional career ladder series. This provides a mechanism whereby outstanding employees of all ethnic backgrounds can compete for positions that afford them promotion potential.

OTHER MINORITY EFFORTS

Mr. Stokes: How many and what percentage of employees of your institute are minorities? Please provide a breakdown by race and grade level.

Dr. Kirschstein: Of the Institute's 206 employees, 58 are minorities. The number and percent of minority employees, by race and grade level follow:

RACIAL BREAKDOWN OF NIGMS STAFF

GS Grade	Total Number of Employees	African American		Caucasian		Asian/ Pacific Islander		Native American		Hispanic	
		#	%	#	%	#	%	#	%	#	%
3	1	0	0	1	100	0	0	0	0	0	0
4	16	6	38	10	62	0	0	0	0	0	0
5	16	6	38	10	62	0	0	0	0	0	0
6	20	8	40	12	60	0	0	0	0	0	0
7	26	6	24	18	69	2	8	0	0	0	0
8	6	2	33	4	66	0	0	0	0	0	0
9	16	4	25	11	68	1	6	0	0	0	0
10	1	0	0	1	100	0	0	0	0	0	0
11	3	1	33	1	33	1	33	0	0	0	0
12	17	2	12	14	82	1	6	0	0	0	0
13	3	0	0	3	100	0	0	0	0	0	0
GM Grade											
13	13	1	8	11	84	0	0	0	0	1	8
14	19	3	16	12	63	1	5	0	0	3	16
15	18	3	17	14	77	0	0	0	0	1	6
SES	6	0	0	6	100	0	0	0	0	0	0
Comm Ofcr	3	0	0	3	100	0	0	0	0	0	0
Expert	2	1	50	1	50	0	0	0	0	0	0
Stay in School and PRATs	20	1	5	16	80	2	10	0	0	1	5

Mr. Stokes: How many are employed in a research capacity?

Dr. Kirschstein: As you know, the Institute has primarily an extramural focus with the majority of its professional staff performing research administration functions, i.e. review or grants administration. Of these research administrators, 12 are minorities.

The Institute has a very small intramural research program called the Pharmacological Research Associate Training (PRAT) Program. One of the 19 PRAT scientists is a female Pacific/Islander.

Mr. Stokes: Please describe for the Committee the resources and funding levels which will be provided for minority-specific research activities in FY 1993.

Dr. Kirschstein: From the NIGMS appropriation, $51.8 million will support various minority-specific grant programs, including MBRS, MARC, research supplements for minorities, and the special predoctoral fellowships and bridging programs. Other components of NIH will also provide $18.6 million toward the support of NIGMS-administered programs aimed at increasing the participation of underrepresented minorities in biomedical research. Thus, the FY 1993 total funding for NIGMS-administered minority-specific research activities will be $70.4 million. With regard to resources, NIGMS devotes at least 28 full-time equivalent staff years to the stewardship and direction of these activities. About $2.2 million of the NIGMS overhead budget pays their salaries and benefits and provides funding for overhead expenses associated with mounting these activities.

Mr. Stokes: How do these levels compare to last year's levels?

Dr. Kirschstein: With regard to the grant programs, from the NIGMS FY 1992 appropriation, $51.8 million will support minority-specific research and research training grant programs. Including support from other components of NIH, the FY 1992 for these programs is $67.1 million.

Mr. Stokes: The total funding represents what percentage of your budget?

Dr. Kirschstein: The $51.7 million represents 6 percent of the total NIGMS budget.

Mr. Stokes: To what extent are you working with the Office of Minority Health to effectuate these goals?

Dr. Kirschstein: Our interactions take several forms. We keep Dr. Ruffin, the director of the Office of Minority Health, informed about developments regarding the programs which NIGMS administers and often include him in meetings in which the agenda includes discussion of matters relating to NIGMS minority-specific activities. He, in turn, discusses matters with us as appropriate. Recently, Dr. Ruffin asked NIGMS to work with him to design and announce two new programs to address specific portions of the research training pipeline for minorities. One of these will bridge the transition from two-year or junior colleges to four-year institutions awarding the Bachelor of Science degree. The other will bridge the transition from the terminal Masters Degree in the Sciences to Ph.D.-granting programs. Dr. Ruffin has provided $2 million in FY 1992 for these two bridging programs. NIGMS expects to cooperate with the Office of Minority Programs on other activities of mutual interest in the future.

BASIC RESEARCH

Mr. Early: Many scientists comment on the importance of basic research to the broad health-related research enterprise. In addition many articles in newspapers and magazines seem to feature important developments in studies of genes or cells or such things as antibodies and hormones that might hold real promise for helping us prevent or treat diseases. NIGMS is the home of basic research at NIH.

Has your Institute received the resources in the FY 1993 budget and in recent years to protect and enhance the contribution of basic research to the rest of the research enterprise?

Dr. Kirschstein: The research grant budget of the NIGMS has increased in recent years, and would increase again in the proposed FY 1993 budget, at about the same rate as the overall NIH research grants budget which provides two percent real growth over FY 1992. This means that the basic research supported by the Institute constitutes about the same share of the biomedical research enterprise as it has in recent years.

Mr. Early: In what areas of science is NIGMS investing the most?

Dr. Kirschstein: NIGMS is investing most of its funds in research in molecular medicine--primarily in fundamental genetics, molecular and cellular biology, and chemistry. These areas dominate the NIGMS grant portfolio. An increasing and significant share now also goes to research in structural biology. This research usually pays off in two ways--by yielding research techniques and approaches that are widely applicable in the more targeted research supported by the rest of NIH or performed by industry, and by generating specific knowledge about life processes, health and disease at their most basic level.

Mr. Early: What should be the payoffs of these investments in the research supported by other institutes of NIH?

Dr. Kirschstein: We expect NIGMS supported research to continue to provide the fundamental knowledge about the function of cells and other biological systems that are important for the understanding of health and diseases. Research on cancer, heart disease, mental retardation, and countless other disorders benefits from that fundamental knowledge. In addition, NIGMS-supported research will continue to contribute directly to the growth of the biotechnology industry through this fundamental knowledge and through the development of such techniques as recombinant DNA technology that has revolutionized modern biology. Other techniques permit the manipulation of biological systems, a necessity both in the biotechnology industry and in the research supported by other institutes of NIH.

BIOTECHNOLOGY

Mr. Early: Much has been made of the priority given to biotechnology in this proposed budget, and NIH's role in this biotechnology area has been highlighted. What is the role of NIGMS in supporting biotechnology?

Dr. Kirschstein: NIGMS is the lead Institute at NIH in the support of biotechnology. In the research training arena, the Institute's traditional multidisciplinary research training grants provide the manpower needed by the biotechnology industry in the fundamental areas of biochemistry, structural biology, cell and molecular biology, genetics, and pharmacology. In addition, since 1989, the Institute has had a specialized research training program in biotechnology. This program prepares scientists to apply their training in engineering, physics, mathematics, chemistry, and biology to areas of biomedical research related to biotechnology. Trainees typically participate in internships in the laboratories of biotechnology companies. In addition, NIGMS supports the fundamental research upon which the biotechnology industry draws for its progress. For example, NIGMS supported the key experiments, performed by Cohen and Boyer, leading to the development of recombinant DNA technology. This technology, in turn, led to the establishment of the biotechnology industry.

Because of its long record of support for biotechnology, NIGMS has played the lead role in preparing the Biotechnology portion of the NIH Strategic Plan. We are now planning a meeting in the fall of 1992, to discuss possible new initiatives in biomolecular engineering that will have a major impact on the biotechnology industry.

Mr. Early: Given the high priority placed on biotechnology in the President's presentation of this 1993 budget, have the NIGMS programs been given significant increases?

Dr. Kirschstein: The NIGMS budget increase above FY 1992 is 5.8 percent. Within this amount, funds for research grants are proposed to increase 7 percent. Thus, a slight increase in the research activity in the areas related to biotechnology seems likely.

Mr. Early: Could you offer a few specific examples of research recently funded by NIGMS which already had or will soon have important pay-offs in the biotechnology area?

Dr. Kirschstein: In recent years, our Congressional testimony has pointed to a number of beneficial products bioengineered using recombinant DNA. First, in the health care arena, these include a new hepatitis vaccine, epidermal growth factor, human growth hormone, tissue plasminogen activator (TPA), and interferon. Recombinant DNA technology has also been applied widely in developing improved agricultural products. Second, the pharmaceutical industry is already using a technique discovered by NIGMS grantees which addresses a longstanding problem in drug development. Now, the new technique permits them to manufacture drugs in only the single structural conformation that has beneficial effects. The production has yielded mixtures of two "mirror-image" structures and often one of those not only lacked therapeutic qualities, but also produced toxic effects. Third, the polymerase chain reaction (PCR) technique, now widely used as a diagnostic tool and in the forensic examination of human DNA, was also a product of NIGMS-supported research.

One example of a very recent discovery with significant potential is a class of compounds called "chaperonins." These originally had the rather nondescript title of "heat shock proteins," since they were first found when yeast cells were subjected to heat or other shocks. These proteins more recently were found to have an important function in normally functioning cells, namely transporting other proteins across the cell membrane--hence the name "chaperonins." More recently, it was discovered that they also operate to help proteins fold into their active form within cells. This immediately excited the interest of the biotechnology industry, since many bioengineered proteins do not fold properly, and strenuous, complicated, and expensive efforts are thus required before these proteins will become commercially useful. By introducing the chaperonins into bioengineered organisms, these efforts may no longer be required. This is an example of fundamental research that was not targeted but has emerged as important to the biotechnology industry.

Other, more directed efforts, are in the area of targeted drug design. These studies attempt to use the detailed structures of proteins involved in disease as a basis for the design of drugs. Part of this effort is related to the AIDS research program at NIGMS, and part to the Institute's usual research programs. Although it has not yet been possible to design a completely new drug using these principles, progress is excellent and we expect important pay-offs in the near future.

RESEARCH TRAINING

Mr. Early: Would you explain the role of the NIH-funded research training programs in the preparation of new scientists?

Dr. Kirschstein: Through a variety of programs and mechanisms, the various Institutes of NIH provide support for the training and education of a cadre of scientists who will be leaders in science research and teaching in the next century. In most of the categorical Institutes, research training grant programs support primarily postdoctoral trainees along with a few predoctoral students, and provide training for new scientists largely in research areas relevant to the mission of each of these institutes.

The NIGMS supports about 55 percent of the NIH predoctoral trainees through a program of multidisciplinary training grants in the biomedical sciences. These grants support students, paying for stipends, a portion of their tuition, trainee travel, and research related expenses, and foster the development of excellent multidisciplinary graduate research training at universities throughout the country. Trainees are usually supported directly by the training grant during their first two years of graduate school, and concentrate on advanced courses and laboratory rotations that enable them to receive the broad experiences needed to be productive research scientists. This type of support is critical in the early stage of biomedical graduate training, so that students can benefit from multidisciplinary exposure and not be forced to choose research fields prematurely in order to receive support. These same students are usually supported on research grants or by university teaching research assistantship appointments in their later years in graduate school, years during which they perform the research leading to their doctoral dissertations.

The NIGMS supports postdoctoral students in basic biomedical fields with individual fellowships, and in clinical research fields with institutional training grants. These programs permit doctoral graduates to receive intense and specialized research training that will prepare them for independent and productive research careers.

Mr. Early: Do these programs still warrant the investment or could new scientists be prepared just as well through other means?

Dr. Kirschstein: We believe that these multidisciplinary predoctoral programs are of great importance and are the best way to train new scientists during the early years of their preparation for careers in research. Should graduate students have to be supported solely by research grants, the organized, multidisciplinary research training at institutions supported by the predoctoral training grants would, for the most part, be seriously compromised. Students who have to choose research fields in their first year and be responsible to a single mentor, are less able to learn from the broader based graduate faculty. For young physician researchers, an organized institutional postdoctoral training grant provides the intense fundamental training and research role models needed.

Mr. Early: The 1993 funding request for research training remains the same as the FY 91 and FY 92 funding level. NIGMS is at the forefront of NIH in its support of research training.

Do you have any concerns about the impact of this straight line research training budget?

Dr. Kirschstein: Because research training has always been a major mission of NIGMS, we are somewhat concerned about the fact that the research training budget for FY 1993 is level and does not permit us to expand research training into new developing fields.

Mr. Early: Is NIGMS able to respond to areas where increased research manpower will soon be needed or can you really only keep existing efforts going?

Dr. Kirschstein: It would be difficult for NIGMS to initiate new training programs without additional funds. Most of the NIGMS training grant programs are funded below the Council recommended levels and could not be reduced further without serious damage. Although a very small initiative in research training at the chemistry-biology interface may be undertaken, the NIGMS will be unable to do more than keep our existing programs going without additional funds.

Mr. Early: If additional funds were available for research training, where would you direct them?

Dr. Kirschstein: The FY 1993 budget does provide funds to support our highest research program priority. If additional funds were available, they would be used to increase the level of support for the following: the new training program at the chemistry-biology interface, the Minority Predoctoral Fellowship Program, the Minority Access to Research Careers Honors Undergraduate Research Training Freshman-Sophomore Program, and the Medical Scientist Training Program. In addition, an increase in the trainee stipend level would be a high priority.

Mr. Early: Doctor, both academicians and industry leaders insist that multidisciplinary training of biologists or chemists is needed in order to really capitalize on areas of opportunity ripe for exploitation, particularly in the fields of biotechnology and pharmaceuticals. They also say that few have received this type of training. Do you agree?

Dr. Kirschstein: Yes, I agree. Although the NIGMS has supported predoctoral research training in the biomedical sciences through multidisciplinary training grant programs since 1975, and many scientists in biomedical research fields have benefitted from the research training sponsored by these programs, few have come from the research fields at the chemistry-biology interface.

Mr. Early: What steps is NIGMS taking to address this situation?

Dr. Kirschstein: To assess the need for multidisciplinary research training in this area, the NIGMS sponsored a workshop in December 1991. Fifteen participants from both academia and industry attended and advised us of the many opportunities for scientific breakthroughs in this field at the chemistry-biology interface and of the expected benefits both to academia and to the pharmaceutical and biotechnological industries. They recommended that NIGMS consider initiating a formal research training program in this area as soon as possible. After discussing the workshop recommendations with the National Advisory General Medical Sciences Council, NIGMS decided to move forward in a measured way. Thus, the Institute has just announced a new multidisciplinary predoctoral research training program--"Chemistry-Biology Interface Predoctoral Training." We are exploring possible partnerships with industry to mount this program.

Mr. Early: Are funds included in your budget request for this purpose?

Dr. Kirschstein: The proposed budget was developed prior to the decision to try to begin a training program at the chemistry-biology interface. However, NIGMS will reallocate some funds to begin such a program should response to the announcement warrant this.

Mr. Early: Is the NIH planning to increase trainee stipends for either FY 92 or FY 93?

Dr. Kirschstein: The proposed 1993 budget does not include a provision for a stipend increase. After a four-year freeze, predoctoral stipends were increased in 1989 from $6,500 to $8,500. This stipend was increased again in 1991 to $8,800 and a similar 4 percent stipend had been proposed in the budget increase for 1992. The amount finally appropriated for research training did not permit this increase.

Mr. Early: If so, how do you plan to increase the number of trainees as well as stipends with no increase in funds?

Dr. Kirschstein: With no increase in the research training budget of FY 1993, the NIGMS will not be able to increase the number of trainees or to increase the stipend level.

RESEARCH PROJECT GRANTS

Mr. Early: While the total number of research grants funded by NIGMS appears to be rising from 1991 to 1992 and proposed in 1993, the number of competing grants NIGMS would fund in 1993 would be significantly lower than in either 1991 or 1992. Could you provide your assessment of the general impact of these year to year variances?

Dr. Kirschstein: In FY 1991, the Institute was able to fund a larger number of competing awards, primarily because the NIH Cost Management Plan was implemented. While we were pleased with the number of new awards we were able to make, they obviously generated a large commitment base for FY 1992 and FY 1993, thus reducing the amount of funding available for competing awards in FY 1992 and FY 1993. It has long been a goal of the Institute, and of NIH, to provide for a stable, consistent number of new and competing awards, in part because this makes competition for research grant support equitable from year to year. In order to provide this stability to the extramural community, avoiding "peaks" and "valleys," or year to year variances in the funding of new grants is desirable.

Mr. Early: What is your assessment of the particular consequences in 1993 for addressing areas of research opportunity in the basic science supported by the Institute?

Dr. Kirschstein: As you noted, at the current level of funding, the number of competing grants NIGMS would fund in FY 1993 would be significantly lower than in either FY 1991 or FY 1992. Thus, there will be a significant number of outstanding research grant applications, in all the areas of research supported by NIGMS, that will not be funded. In particular, however, there are areas in the field of biotechnology, such as biomolecular engineering and rational drug design, upon which the Institute will not be able to fully capitalize. In addition, the fields of cellular and molecular research, specifically those that relate to the mechanisms of regulation and control of cell division, will not be fully investigated.

Mr. Early: What percentage of new and competing grants will the Institute fund under the FY 93 budget request, and how does this compare to FY 92 and FY 91?

Dr. Kirschstein: Commensurate with the adoption of the Cost Management Plan, we no longer calculate award rates, but only success rates.

Mr. Early: How does this compare to the award rate of five years ago? Ten years ago?

Dr. Kirschstein: The award rate was 40 percent five years ago in FY 1988 and 41 percent ten years ago in FY 1983.

Mr. Early: What is the projected "success rate" for your Institute and how does this compare to FY 91 and FY 92?

Dr. Kirschstein: The estimated success rate for FY 1993 is 27 percent. This compares to an estimated success rate of 31 percent in FY 1992 and 34 percent in FY 1991.

Mr. Early: What success rate would you like to see in order to fund an appropriate number of the exciting and most promising research proposals coming out of your Institute?

Dr. Kirschstein: In my professional judgment, it would take a success rate of approximately 40 percent to fund the truly promising research applications received by NIGMS. Even at this success rate, there would still be meritorious research proposals that would remain unfunded.

Mr. Early: To what payline percentile will the Institute be able to fund under the budget request and how does this compare to FY 92 and FY 91?

Dr. Kirschstein: The estimated payline percentile for NIGMS is 21 percent in FY 1993. This compares to an estimated payline percentile of 26 percent in FY 1992 and a payline percentile of 29 percent in FY 1991.

Mr. Early: Would you tell us what the trend has been in these areas for your Institute?

Dr. Kirschstein: Through most of the 1980's, our success rate was generally between 35-40 percent of reviewed applications. We consider this an optimal level of funding for the excellent research proposed by our grantees. This ratio dropped to 28 percent in 1989 and 22 percent in 1990, but has increased to 34 percent and 31 percent in 1991 and 1992, respectively. In FY 1993, we expect the success rate to be 27 percent.

RPG'S--AVERAGE COST INCREASE

Mr. Early: What was the downward adjustment for noncompeting grants in FY 91 and FY 92?

Dr. Kirschstein: FY 1991 was the first year of the implementation of the NIH Cost Management Plan. In order to fund an adequate number of new and competing awards in the first year of the Plan, the amount of the typical noncompeting grant averaged 10.4 percent below that recommended by the initial review groups; however, this generally represented a four percent increase above the previous year's level.

Since an underlying principle of the Cost Management Plan is the payment of noncompeting grants at committed levels, we expect to fully meet noncompeting commitments both in FY 1992 and in future years.

Mr. Early: What are you projecting for FY 93?

Dr. Kirschstein: In concert with the Cost Management Plan, no reductions to noncompeting grants are anticipated in FY 1993.

Mr. Early: Will the Institute be able to fund noncompeting research project grants at commitment levels and new and competing research grants at peer reviewed levels?

Dr. Kirschstein: As mentioned above, no reduction in noncompeting grants is anticipated in FY 1993 if the Institute receives the amount requested in the President's Budget. However, in order to provide for a reasonable number of new and competing research project grants in FY 1993 and to adhere to the policy, to which Congress and NIH have agreed, that competing grant costs not increase more than the Biomedical Research and Development Price Index, the budget of each new and competing application will be analyzed by Institute staff, after the initial study section and Council review. Similar to previous years, the outcome is most likely to be a level below that recommended by peer review. These reductions are likely to be in the 15% range.

Mr. Early: Does this concern you, Doctor?

Dr. Kirschstein: While we are pleased to be able to provide the stability and predictability that is so necessary for our noncompeting grantees and still fund a number of new and competing applications, we recognize that one result of our efforts to achieve this goal may be slower progress on research projects.

RESEARCH CENTERS

Mr. Early: What role do centers play in the NIGMS research mission?

Dr. Kirschstein: NIGMS funds research centers in several specialized areas--pharmacology, anesthesiology, and trauma and burn research--where close collaboration between basic and clinical scientists is likely to yield results that would not be as likely to emerge from either working alone.

Mr. Early: What is the average increase in a center grant under the budget request?

Dr. Kirschstein: The FY 1993 budget proposes no increase in the average size of a research center grant over 1992.

Mr. Early: What was the level of downward adjustments in the centers' program in FY 1991 and FY 1992? and what is the estimate for FY 1993?

Dr. Kirschstein: In FY 1991 the amount awarded for the average competing center grant was 8.6 percent below that recommended by the initial review groups. In FY 1992, there were no adjustments of this kind, on average. In FY 1993, the average center award is estimated to be 4 percent below the amount calculated under the cost management principles.

Mr. Early: Funding for centers has not increased very much over the past few years. What impact is this having on research programs at these centers?

Dr. Kirschstein: For many years, NIGMS has had an announced policy of limiting both the single year and the total multi-year costs of research center grants. This means that scientists who apply for center grant support from NIGMS must design their research projects with these limits in mind. Thus, when NIGMS has awarded less than the amounts recommended by the peer review groups, progress in the work described in the applications may be slowed.

FINANCIAL MANAGEMENT PLAN

Mr. Early: Is the NIGMS making greater use of "out of order" funding to achieve a lower cost per award?

Dr. Kirschstein: Our cost management strategies have been effective in achieving a lower cost per award. The major reason for "out of order funding" recommendations made by the NIGMS Council or staff is to "reach for" projects just beyond the payline which are particularly innovative, risky, or scientifically novel or for which the scientist has no other source of support.

Mr. Early: What effect has limiting the overall average increase in the cost of a grant had at your Institute? Is there any indication that Boards and Councils are becoming conservative?

Dr. Kirschstein: By implementing the NIH cost management plan with regard to competing grants, in FY 1991, we were able to fund 130 additional competing awards and increase our success rate from 29 to 34 percent. In FY 1992, we project that our cost management strategy will allow us to make 113 more competing awards and increase our success rate from 27 to 31 percent. Our plans for FY 1993 project an increase of 127 competitive awards, and an increase from 22 to 27 percent in the success rate. The National Advisory General Medical Sciences Council led the way in FY 1990 in recommending that cost management strategies be used in determining award levels. Their intent was to balance the rate of growth with the need to fund as many new and innovative projects as possible. They continue to advise us regarding the proper balance point.

OTHER

Mr. Early: Doctor, there is a significant decline (from 151 to 36) in the number of awards anticipated in FY 1992 in the other research category designated "other." Why is there such a sharp decrease, and what types of activities will be curtailed or eliminated?

Dr. Kirschstein: The decline in the number of grants will occur primarily in the Small Instrumentation Program and in the conference grants that can be funded. Since the proposed budget gives highest priority to research project grants, growth in funding of other grant mechanisms is limited.

NIGMS PROFESSIONAL JUDGMENT BUDGET

Mr. Early: What was the NIGMS Professional Judgment Budget and how does it differ from the request before us?

Dr. Kirschstein: The NIGMS Professional Judgment Budget for FY 1993 was $1,029 million. This level would have provided a 40 percent success rate for competing research grants and would have funded 6,232 research trainees, each receiving a significant stipend increase. In addition, several initiatives aimed at increasing the number of underrepresented minorities in biomedical research would have been expanded. The President's budget for FY 1993 proposes $862 million. This would provide a 27 percent success rate for competing research grants and would fund 4,232 research trainees with no stipend increase.

RESEARCH INITIATIVES

Mr. Early: Will any significant new research initiatives be lost or delayed by lack of funds in the FY 1993 budget request?

Dr. Kirschstein: At the current level of funding, only about 27% of research project grant applications will be funded at NIGMS. This means that some research proposals of high merit will be lost or delayed. However, the President's budget supports those projects of highest merit. As you know, in science our opportunities for research far outstrip our resources and it is our challenge to fund only the very best research projects.

PRIORITIES AND ADDITIONAL NEW FUNDS

Mr. Early: What priorities would the Institute pursue if additional resources were available? If an increase over the FY 1993 request is provided, how would you use these additional funds?

Dr. Kirschstein: The Institute would target three priority areas. First, we would attempt to move toward funding between 35 and 40 percent of research grant applications, consistent with our historical average. This would permit us to support additional cutting-edge research in each of our program areas. We would also enhance our programs which are designed to increase the numbers of underrepresented minorities pursuing careers in biomedical research. Finally, we would pursue a number of initiatives related to biotechnology, particularly by initiating a research training program at the chemistry-biology interface and by beginning a research program in the area of biomolecular engineering. The Institute is planning a meeting in the fall of 1992 to assess the state of research in this promising area and to discuss which fields are most ripe for opportunity at this time.

RESEARCH PROGRAMS

Mr. Early: The justification seems to indicate that biotechnology and structural biology provide opportunities for rational drug design. What can we look forward to in this area of research?

Dr. Kirschstein: The rapid development of techniques in structural biology make it possible to get a detailed three-dimensional picture of many proteins and nucleic acids. Since many, and perhaps most, drugs act by affecting these molecules, it would be both more scientifically sound, as well as more cost effective, to design drugs by directly modeling them to bind to or fit onto a part of the protein, rather than by a random screening process, as is currently done. Many theoretical and experimental problems need to be solved before this is possible, but progress has been very promising and I believe that we will be at a point in the next few years where many drugs will be designed and produced using such rational drug design techniques.

Mr. Early: I understand that several new technologies will play significant roles in both basic research and biotechnology. Among these are electrospray technology and ligase chain reaction, which you mentioned in your statement. What will these technologies enable research scientists to do?

Dr. Kirschstein: Electrospray technology is an adjunct to the technique of mass spectrometry that allows very small amounts of large molecules such as proteins to be sequenced rapidly, accurately, and efficiently. This technique will particularly benefit investigators who are attempting to engineer proteins for specific uses, and who wish to quickly evaluate the structure of the proteins they are manufacturing. In addition, it will benefit scientists who are isolating very small quantities of material from cells and who require sequences to identify them.

The ligase chain reaction is a modified version of the now-familiar polymerase chain reaction, which can amplify very small quantities of nucleic acids. In contrast to the polymerase chain reaction, it can pick up much smaller changes in DNA, and consequently can be used more effectively for diagnostic purposes.

Mr. Early: Are there any particular areas where you now expect major advances because of the availability of these new technologies?

Dr. Kirschstein: It is entirely feasible that the ligase chain reaction (LCR) will be invaluable in genetic screening, particularly as a tool in screening simultaneously for a variety of mutations. It is also possible that by combining the polymerase chain reaction (PCR) and LCR, a new era of DNA diagnostics will be introduced.

Electrospray technology will allow researchers to work more rapidly and with smaller quantities of materials. This will be especially useful in the analysis of toxins and venoms.

PHARMACOLOGICAL SCIENCES

Mr. Early: Your institute supports a research program in pharmacological sciences. What major advances have there been in this field of research within the past few years?

Dr. Kirschstein: Our research program in pharmacological sciences encompasses not only pharmacology, but also research in anesthesiology and biorelated chemistry. I am pleased to be able to give you some examples of major advances in each of those areas:

° Just this year, Dr. Stuart Schreiber of Harvard University made a major discovery regarding the action of how two drugs used extensively to suppress rejection of transplanted organs, namely cyclosporin and FK-506. While these two compounds do not have immunosuppressant activity themselves, when they bind to receptor proteins called immunophilins, the drug-immunophilin complex exhibits immunosuppressant activity. Not only does this discovery help us understand how these drugs suppress the immune system so that their safety and efficacy can be improved, but it also provides immunologists with a tool to study early steps in the immune process.

° In the area of chemistry, Dr. Barry Sharpless has recently devised a new organic synthetic methodology which produces a single stereoisomer of compounds that exist as multiple stereoisomers, or "mirror images." His technique is already in use in the pharmaceutical industry and promises to have wider applicability in the insecticide, flavor, and fragrance industries.

This process, in conjunction with the development, by Nobel Laureate Dr. E.J. Corey, of the group of totally synthetic catalytic molecules he calls chemzymes, promises to have a major beneficial economic and safety impact on those industries whose products might be stereoisomers.

- For over a hundred years, people have thought of anesthetics as acting nonspecifically to disrupt cell membranes and thus cause their anesthetic effects. This lack of specificity has not allowed much room for scientists to attempt to design safer and more effective anesthetic agents. Within the last 3 years, compelling evidence has been found in several NIGMS-supported laboratories that anesthetics do indeed have a specific cellular binding site, possibly even a specific receptor, that mediates their anesthetic activity. This is the crucial first step not only in designing safer and more efficacious anesthetic agents but also in finding out why certain people exhibit unusual and severe side reactions to this class of drugs.

- We have often reported to you of our excitement about the field of G proteins, those molecules responsible for binding guanosine triphosphate (GTP) and transducing signals across cell membranes. Work by Dr. Henry Bourne of the University of California, San Francisco, has shown that a point mutation in the alpha subunit of one of these G proteins from the pituitary resulted in uncontrolled growth of a pituitary gland tumor. Subsequently he found that related mutations in other G protein alpha subunits were associated with oncogenes present in thyroid, adrenal cortex and ovarian tumors. This work has now been transferred to the National Cancer Institute because of its direct relevance to its mission.

These are just a few examples of the Pharmacological Sciences Program-supported research which has produced major advances in the areas of pharmacology, anesthesiology, and biorelated chemistry.

Mr. Early: Doctor, are there any collaborative efforts or is there any interaction between your Pharmacological Sciences Program and the National Institute of Drug Abuse?

Dr. Kirschstein: While there are not any formal collaborative efforts between the Pharmacological Sciences (PS) Program and the National Institute of Drug Abuse (NIDA), there is significant interaction between the two in several different areas. The guidelines by which research grant applications are assigned delineate quite clearly that applications which are directed towards the pharmacology of drugs of abuse or modulation of pain by narcotics are assigned to NIDA and these guidelines were arrived at through discussions between the staff of our PS Program and NIDA. Certain research grant applications which focus on the interactions between drugs of abuse and their putative receptors but which also have more general pharmacological ramifications, are assigned dually to both institutes. If the application is fundable, then we conduct negotiations to determine which institute is more appropriate to fund the application. In addition, the Pharmacology Research Associate (PRAT) Program has 4 preceptors located in the NIDA intramural program and currently there are 2 PRAT fellows working in two of these laboratories.

STRATEGIC PLAN

Mr. Pursell: Where does the NIGMS fit into the NIH strategic plan?

Dr. Kirschstein: Because the framework of a strategic plan that appears to be taking shape features the areas of molecular medicine, structural biology, and biotechnology, it is likely that most of the areas of research and research training that NIGMS supports will be addressed in the plan that emerges. The research funded by several of the Institute's programs, especially by the Genetics and Cellular and Molecular Basis of Disease Programs, is aimed at discovering the causes of and remedies for disease at the molecular and cellular level, just as is envisioned in the proposed molecular medicine thrust of the plan. Similarly, many of the studies supported by the Biophysics and Physiological Sciences Program lie in the area of structural biology, determining the three-dimensional structures of biologically-important molecules and examining their functional implications. All of NIGMS's programs support research relevant to biotechnology. Indeed, NIGMS plays a preeminent role at NIH in biotechnology since most of the research it supports yields information fundamental to advances in a wide range of fields of interest to biotechnology, including rational drug design, protein engineering, and genetic techniques. Because NIGMS is heavily involved in research training, the Institute also expects to be a key player in defining the needs for intellectual capital as the strategic plan evolves.

SCIENCE EDUCATION

Mr. Pursell: What educational programs does the institute have to take biomedical research into the classroom?

Dr. Kirschstein: There are several formal and informal educational programs through which the NIGMS exposes students to biomedical research. As part of its information dissemination mission, a series of brochures have been developed by the Institute's Office of Research Reports. These brochures are mailed to high-school and undergraduate science teachers and students upon request. In FY 1991, approximately 20,600 brochures were distributed.

In addition, approximately nine of the Institute's professional staff are participating in an NIH-wide science education effort called "Science Alliance." In fact, NIGMS staff have been instrumental in developing this project in which NIH scientists are teamed with teachers and students at local elementary schools. Scientists support the teachers in the school by participating in science classes, serving as role models for students, by serving as sources of scientific information, and by bringing their enthusiasm to the classroom. Some of the goals of the Science Alliance program are to: increase enthusiasm for science among teachers and students; increase teachers' confidence in using the science curricula and materials; integrate science with other subjects; and identify talented young people.

One NIGMS staff member participates in a Montgomery County initiative called "Hands-On Science", in which she teaches two one-hour courses in science to elementary students. Finally, several NIGMS professional staff participate in a variety of voluntary visits to elementary and secondary schools to acquaint students with the field of biomedical research and to participate as judges in science fairs.

OUTREACH PROGRAMS

Mr. Pursell: What outreach programs is the Institute undertaking to be more responsive to the community?

Dr. Kirschstein: As you know, the NIGMS differs from most of the other Institutes, Centers, and Divisions (ICDs) at NIH because its primary mission is the conduct of basic biomedical research. Thus, the outreach programs it conducts differ from the more traditional outreach programs that focus on education and prevention aspects of a particular disease. However, in FY 1992, in an effort to be more responsive to its minority community, a comprehensive workshop was developed that would increase the number of predominantly minority institutions aware of and competitive for MARC and MBRS funding. The first of a series of such workshops was held in Charlotte, North Carolina, for approximately 22 institutions. Two additional regional workshops were originally planned for FY 1992 but could not be held because of the severe constraints on the Institute's travel budget. These will be held next fiscal year, travel funds permitting.

In November 1991, the Institute hosted a combined MARC/MBRS Symposium that brought together almost 1,800 minority students, researchers, and representatives from academia and industry to facilitate the interactions of the students with those individuals most capable of assisting them in achieving their career goals in biomedical research. This outreach effort is a part of the Institute's commitment to increasing the number of underrepresented minorities in biomedical research.

Other NIGMS outreach programs are described in the response to the preceding question, that is, "The Science Alliance" project, the "Hands-On Science" project, and the information brochures distributed by the Institute.

INTERACTIONS WITH THE PRIVATE SECTOR

Mr. Pursell: How does the Institute interact with the private sector, especially the pharmaceutical industry?

Dr. Kirschstein: The Institute interacts with the private sector in several ways. Several NIGMS staff serve on industry-academic interface committees. For example, Dr. Christine Carrico, Director of the Pharmacological Sciences Program and I both attend the meetings of the Drug Development Forum, sponsored by the Institute of Medicine/National Academy of Sciences, the Pharmaceutical Manufacturers Association, and the Food and Drug Administration. Dr. Marvin Cassman, Deputy Director of the Institute, and Dr. Michael Rogers, Deputy Director of the Pharmacological Sciences Program attend meetings sponsored by the Board on Chemical Sciences and Technology of the National Research Council.

The Institute relies on representatives from industry for advice and consultation. For instance, it is customary for the Institute to have at least one representative from industry on the

National Advisory General Medical Sciences Council. Dr. Paul Anderson, Vice President for Chemistry of Merck Sharp and Dohme, Inc., currently fills this role. Other members of industry serve as members of NIGMS peer review groups. In addition, private sector representatives are usually included when special advisory groups are convened regarding proposed new initiatives. One example of this is the working group recently convened to discuss the need for a new Chemistry-Biology Interface training initiative on which there were representatives from two major drug companies.

Finally, one distinctive feature of the Institute's Biotechnology Training Program is the requirement for trainees to serve an internship with a biotechnology company. Monitoring of this requirement, as well as general oversight of the program, requires periodic interactions with the private sector.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

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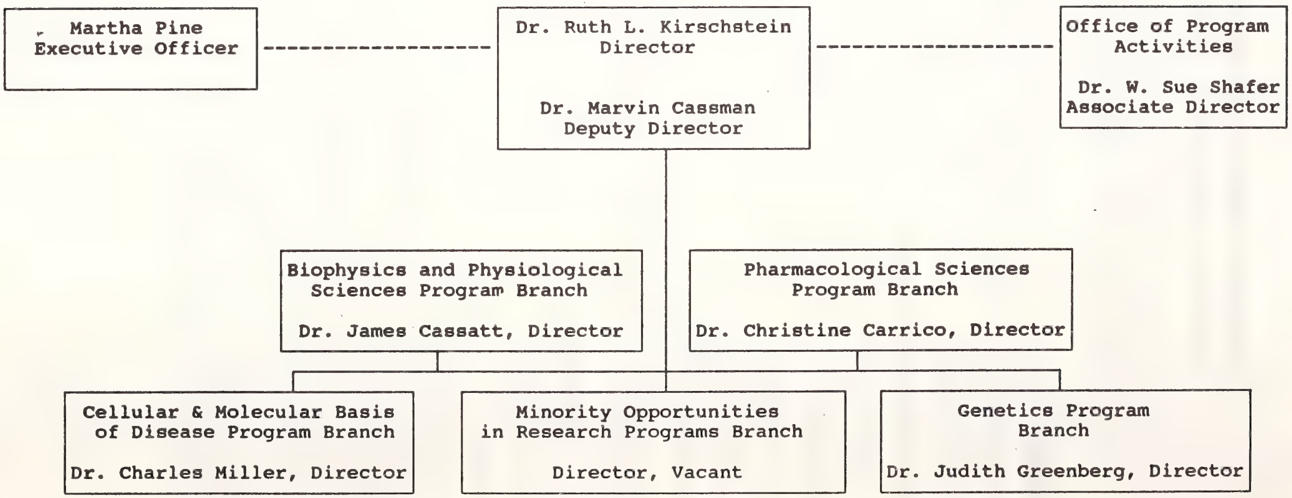
Organization Structure



Martha Pine
Executive Officer

Dr. Ruth L. Kirschstein
Director

Dr. Marvin Cassman
Deputy Director

Office of Program Activities

Dr. W. Sue Shafer
Associate Director

Biophysics and Physiological Sciences Program Branch

Dr. James Cassatt, Director

Pharmacological Sciences Program Branch

Dr. Christine Carrico, Director

Cellular & Molecular Basis of Disease Program Branch

Dr. Charles Miller, Director

Minority Opportunities in Research Programs Branch

Director, Vacant

Genetics Program Branch

Dr. Judith Greenberg, Director

NATIONAL INSTITUTES OF HEALTH

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For carrying out section 301 and title IV of the Public Health Service Act with respect to general medical sciences, [$818,910,000]: $862,069,000: Provided, That of the funds made available under this heading, [$48,104,000] $55,049,000 shall not become available for obligation until September 30, [1992] 1993.

(Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 1992.)

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NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Amounts Available for Obligation 1/

	1991 Actual	1992 Appropriation	1993 Estimate
Appropriation	$779,250,000	$818,910,000	$862,069,000
Sequester Order	-10,000	---	---
Section 514(a) reduction	-460,000	---	---
Section 514(b) reduction	-18,780,000	---	---
Section 214 travel reduction	---	-58,000	---
Section 513(a) travel reduction	---	-95,000	---
Section 513(a) S & E reduction	---	-1,123,000	---
Subtotal, adjusted appropriation	760,000,000	817,634,000	862,069,000
Real transfer from NCI for cancer research	---	1,500,000	---
Real transfer from other Accounts for Shannon Awards	1,283,000	---	---
Comparative transfer to NLM for GENBANK	-3,400,000	-4,000,000	---
Subtotal, adjusted budget authority	757,883,000	815,134,000	862,069,000
Unobligated balance lapsing	-52,000	---	---
Total, Obligations	757,831,000	815,134,000	862,069,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: FY 1991--$7,224,000; FY 1992--$5,600,000; FY 1993--$5,600,000.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Budget Mechanism

(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	No.	Amount	No.	Amount	No.	Amount
Research grants:						
Research projects						
Noncompeting	2,360	$433,749	2,482	$475,445	2,636	$530,640
Admin. supplemental	(41)	1,782	(17)	652	(17)	674
Competing						
Renewal	477	102,638	480	109,918	409	99,464
New	391	54,783	419	62,477	400	63,340
Supplemental	6	668	6	711	5	630
Subtotal, competing	874	158,089	905	173,106	814	163,434
Subtotal, research projects	3,234	593,620	3,387	649,203	3,450	694,748
Research Centers						
Pharmacological sciences	2	1,634	2	1,733	2	1,733
Anesthesiology	1	807	1	858	1	858
Trauma and burn	6	4,483	6	4,519	6	4,519
Subtotal research centers	9	6,924	9	7,110	9	7,110
Other research						
Research career program	19	1,100	20	1,168	20	1,168
MBRS	96	31,614	98	33,059	98	33,059
Other	151	6,919	36	2,776	36	2,776
Subtotal, other research	266	39,633	154	37,003	154	37,003
Total, research grants	3,509	640,177	3,550	693,316	3,613	738,861

Training:						
Individual awards						
Noncompeting	290	7,179	413	10,307	316	7,625
Competing						
Renewal						
New	274	6,391	151	3,734	248	6,416
Subtotal, individual	564	13,570	564	14,041	564	14,041
Institutional awards						
Noncompeting	3,026	65,818	2,987	62,880	3,482	73,533
Competing						
Renewal	480	10,133	681	15,159	186	4,506
New	63	1,402				
Supplementals	82	1,157				
Subtotal, institutional	3,651	78,510	3,668	78,039	3,668	78,039
Total, training	4,215	92,080	4,232	92,080	4,232	92,080
Research and development contracts	6 FTEs	1,827	6 FTEs	1,423	6 FTEs	1,423
Intramural research	18	1,082	22	1,237	22	1,300
Research management and support	165	22,717	170	27,078	171	28,405
TOTAL	183	757,883	192	815,134	193	862,069

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

CROSSWALK - 1992 APPROPRIATION

(Dollars in thousands)

	Research Grants			Training Programs		Research and Development Contracts	Intramural Research	Research Management & Support	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional				
Cellular and molecular basis of disease	$204,178		$948	$2,151	$16,164	$35			$223,476
Genetics	214,834		503	4,852	8,234	1,107			229,530
Pharmacological sciences	104,356	$2,591	333	2,234	12,542	10			122,066
Biophysics and physiological sciences	125,835	4,519	2,160	1,568	29,723	271			164,076
Minority opportunities in research:									
Minority biomedical research support			33,059						33,059
Minority access to research careers				1,844	11,376				13,220
Special minority initiatives				1,392					1,392
Intramural research							$1,237		1,237
Research management and support								$27,078	27,078
Total	649,203	7,110	37,003	14,041	78,039	1,423	1,237	27,078	815,134

NATIONAL INSTITUTES OF HEALTH

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CROSSWALK - 1991 ACTUAL

(Dollars in thousands)

	Research Grants			Training Programs		Research and Development Contracts	Intramural Research	Research Management & Support	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional				
Cellular and molecular basis of disease	$188,015		$2,678	$2,121	$16,194	$29			$209,037
Genetics	197,750		2,593	4,538	8,548	1,517			214,946
Pharmacological sciences	91,324	$2,441	213	2,234	12,542	10			108,764
Biophysics and physiological sciences	116,531	4,483	2,535	1,441	29,850	271			155,111
Minority opportunities in research:									
Minority biomedical research support			31,614						31,614
Minority access to research careers				1,844	11,376				13,220
Special minority initiatives				1,392					1,392
Intramural research							$1,082		1,082
Research management and support								$22,717	22,717
Total	593,620	6,924	39,633	13,570	78,510	1,827	1,082	22,717	757,883

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

CROSSWALK - 1993 ESTIMATE

(Dollars in thousands)

	Research Grants			Training Programs		Research and Development Contracts	Intramural Research	Research Management & Support	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional				
Cellular and molecular basis of disease	$218,555		$969	$2,151	$16,164	$35			$237,874
Genetics	225,161		443	4,852	8,234	1,107			239,797
Pharmacological sciences	112,217	$2,591	333	2,234	12,542	10			129,927
Biophysics and physiological sciences	138,815	4,519	2,199	1,568	29,723	271			177,095
Minority opportunities in research:									
Minority biomedical research support			33,059						33,059
Minority access to research careers				1,844	11,376				13,220
Special minority initiatives				1,392					1,392
Intramural research							$1,300		1,300
Research management and support								$28,405	28,405
Total	694,748	7,110	37,003	14,041	78,039	1,423	1,300	28,405	862,069

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Summary of Changes

1992 Estimated budget authority	$815,134,000
1993 Estimated budget authority	862,069,000
Net change	+46,935,000

	1992 Current Estimate Base		Change from Base	
Changes:	Pos. (FTEs)	Budget Authority	Pos. (FTEs)	Budget Authority
A. Built-in:				
1. Within grade increases		$11,016,000		+$81,000
2. Annualization of pay raise		11,016,000		+116,000
3. One extra day of pay		11,016,000		-43,000
4. Cost of 1992 pay raise		11,016,000		+305,000
5. Increased cost of centrally furnished services		7,844,000		+399,000
6. Service and supply fund increase		4,622,000		+208,000
7. Increased costs of laboratory materials and other supplies		9,455,000		+178,000
8. DHHS Working Capital Fund		788,000		+42,000
Subtotal				+1,286,000
	No.	Amount	No.	Amount
B. Program:				
1. Research projects grants:				
a. Noncompeting	2,482	476,097,000	+154	+55,217,000
b. Competing	905	173,106,000	-91	-9,672,000
Total	3,387	649,203,000	+63	+45,545,000
	Pos. (FTEs)	Budget Authority	Pos. (FTEs)	Budget Authority
2. Research management and support increase	192	27,078,000	+1	+104,000
Subtotal			+1	+45,649,000
Total changes			+1	+46,935,000

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Budget Authority by Activity

(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	FTEs	Amount	FTEs	Amount	FTEs	Amount
Cellular and molecular basis of disease....	---	$209,037	---	$223,476	---	$237,874
Genetics..............	---	214,946	---	229,530	---	239,797
Pharmacological sciences............	---	108,764	---	122,066	---	129,927
Biophysics and physiological sciences....	---	155,111	---	164,076	---	177,095
Minority opportunities in research:						
Minority biomedical research support .	---	31,614	---	33,059	---	33,059
Minority access to research careers..	---	13,220	---	13,220	---	13,220
Special minority initiatives.......	---	1,392	---	1,392	---	1,392
Subtotal...........	---	46,226	---	47,671	---	47,671
Intramural research...	18	1,080	22	1,237	22	1,300
Research management and support.........	165	22,667	170	27,078	171	28,405
Total Obligations...	183	757,831	192	815,134	193	862,069
Unobligated balance lapsing.............		52		---		---
Total, Budget Authority.........	183	757,883	192	815,134	193	862,069
HIV/AIDS...	[2]	[15,588]	[2]	[16,109]	[2]	[17,021]

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Budget Authority by Object

	1992 Appropriation	1993 Estimate	Increase or Decrease
Total number of full-time permanent positions	170	171	+1
Total compensable work years:			
Full-time equivalent employment	193	194	+1
Full-time equivalent of overtime and holiday hours	1	1	---
Average ES salary	$104,000	$107,848	+$3,848
Average GS grade	9.8	9.8	---
Average GS salary	$32,156	$33,345	+$1,189
Average salary, grades established by act of July 1, 1944 (42 U.S.C. 207)	$87,409	$90,643	+$3,234
Personnel compensation:			
Full-time permanent	$7,665,000	$7,993,000	+$328,000
Other than full-time permanent	1,144,000	1,228,000	+84,000
Other personnel compensation	306,000	319,000	+13,000
Special personal services payments	23,000	24,000	+1,000
Subtotal, personnel compensation	9,138,000	9,564,000	+426,000
Personnel benefits	1,871,000	1,959,000	+88,000
Benefits for former personnel	7,000	7,000	---
Travel and transportation of persons	158,000	273,000	+115,000
Transportation of things	50,000	50,000	---
Rent, communications, and utilities	285,000	285,000	---
Printing and reproduction	400,000	400,000	---

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Budget Authority by Object--continued

	1992 Appropriation	1993 Estimate	Increase or Decrease
Other services:			
Project contracts	1,423,000	1,423,000	---
Centrally furnished services	6,783,000	7,065,000	+282,000
Standard level user charge	1,061,000	1,178,000	+117,000
Other	7,447,000	7,809,000	+362,000
Supplies and materials	134,000	134,000	---
Equipment	981,000	981,000	---
Grants, subsidies, and contributions	785,396,000	830,941,000	+45,545,000
Total	815,134,000	862,069,000	+46,935,000

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Significant Items in the House and Senate Appropriations Committee Reports

Minority Initiatives

The House in its report 102-121, page 83 stated "The Committee is concerned that there has been a decline in the percentage of Minority Biomedical Research Support awards going to those colleges and universities for which the program originally was intended. The Committee, in establishing the MBRS Program, intended that predominantly minority institutions, with 50 percent or more enrollment of ethnic-minority students be primary beneficiaries. The Committee requests that the Department initiate a special effort to work with these institutions to enable them to maintain and enhance their involvement with this program."

Action Taken or to be Taken: The National Institute of General Medical Sciences (NIGMS) has planned a series of regional workshops to which representatives of institutions that currently do not participate in the Minority Biomedical Research Support (MBRS) Program will be invited. These institutions are largely Historically Black Colleges and Universities, which are eligible for MBRS support by virtue of the fact that they have enrollments comprised of at least 50 percent ethnic-minority students. These workshops are designed to permit exchange of information regarding the MBRS and other NIGMS programs focused on minority institutions, as well as regarding successful models of program participation. In addition, suggestions regarding how to develop a competitive grant application will be offered. Time on the agenda has been set aside for extensive one-on-one interactions between workshop participants and NIGMS staff. These workshops should facilitate the ongoing dialogue between NIGMS and the institutions which may wish to participate in the MBRS Program. The first of these regional workshops is scheduled to occur in February 1992. Several other workshops will be held in different geographical regions throughout the remainder of the year.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1992 Amt. Authorized	1992 Appropriation	1993 Amt. Authorized	1993 Budget Request
Research and Investigation	Section 301	42 241	Indefinite		Indefinite	
National Institute of General Medical Sciences	Section 461	42 285k 289h	Indefinite	$723,054,000	Indefinite	$769,989,000
National Research Service Awards	Section 487 (d)	42 288	Authorizing legislation is pending 1/	92,080,000	Authorizing legislation is pending 1/	92,080,000
Total Budget Authority				815,134,000		862,069,000

1/ This training authority is shared with the research training programs of the Alcohol, Drug Abuse and Mental Health Administration.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Appropriation History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1984	383,139,000	363,444,000 2/	370,245,000 2/	415,937,000
1985	423,853,000	412.987,000 3/	495,150,000	482,909,000
1986	458,484,000	455,593,000 4/	510,872,000	514,765,000
1986 Sequester	---	---	---	-22,135,000
1987	471,533,000	576,562,000	565,271,000	570,916,000
1988	482,004,000	666,037,000 5/	650,617,000	632,676,000
1989	676,728,000 6/	623,087,000 7/8/	690,653,000 7/	690,653,000
1990	766,421,000 9/	692,639,000 10/	752,939,000 11/	691,278,000 12/
1990 Sequester	---	---	---	-9,496,000
1991	745,494,000 10/	693,499,000 13/10	779,351,000 10/	760,010,000 14/
1991 Sequester	---	---	---	-10,000
1992	833,180,000	820,160,000	815,158,000	818,910,000 15/
1993	862,069,000			

1/ Reflects enacted supplementals, rescissions and reappropriations.

2/ Excludes $48,000,000 in NRSA training programs not considered.

3/ Excludes $48,446,000 in NRSA training programs not considered.

4/ Excludes $57,721,000 in NRSA training programs not considered.

5/ Does not include funding for AIDS research. Consolidated at the Secretary's level.

6/ Does not include funding for AIDS research ($11,100,000). Proposed for consolidation at the Office of the Assistant Secretary for Health.

7/ Includes $11,100,000 for AIDS research.

8/ Excludes $69,841,000 in NRSA training programs not considered.

9/ Excludes funds for AIDS research proposed for consolidation in the Office of the Assistant Secretary for Health. Includes funds for the Human Genome Research Initiative.

10/ Includes funds for AIDS research and the Minority Biomedical Research Support Program which was transferred from the Division of Research Resources. Excludes funds for the Human Genome Research Initiative to be considered under a separate new appropriation account.

11/ Includes funds for AIDS research and funds for the Human Genome Research Initiative.

12/ Includes funds for AIDS research. Excludes funds for the Minority Biomedical Research Support Program which was transferred from the Division of Research Resources, the Human Genome Research Initiative and an enacted administrative reduction of $588,000.

13/ Excludes $85,650,000 in NRSA training programs not considered.

14/ Excludes enacted administrative reductions of $19,240,000 and funds transferred from other accounts for the Shannon awards.

15/ Excludes enacted administrative reductions of $1,276,000.

Justification

National Institute of General Medical Sciences

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
183	$757,883,000	192	$815,134,000	193	$862,069,000	+1	+$46,935,000

General Statement

The National Institute of General Medical Sciences (NIGMS) supports studies that increase understanding of basic life processes. This research is essential in building the foundation of knowledge necessary to enable scientists to tackle a host of specific health problems. Basic research also has significant economic payoffs. It can save health care costs by providing methods to prevent or cure diseases, or ways to treat them more effectively.

Basic biomedical research benefits the economy more directly, as well. The biotechnology industry, for example, grew out of years of research on the genetics of simple organisms such as viruses and bacteria. These studies led to the development of recombinant DNA technology, which permits scientists to produce previously scarce biological or chemical agents such as human insulin, growth hormone, erythropoietin, tissue plasminogen activator, and interferon. Moreover, many nonbiomedical industries, such as agriculture and food processing, have been enhanced by the application of biomedical research findings, and the potential for future applications is tremendous.

The pharmaceutical industry is a major beneficiary of advances in biotechnology and in another area of basic research, structural biology. Knowledge of the structure of a virus, for instance, can provide a target for the rational design of drugs to fight that virus. Designing a drug in this way might save half of the $231 million that the Pharmaceutical Manufacturers Association estimates it costs to bring a new drug to market.

NIGMS funds research in four scientific areas: biophysics and physiological sciences, cellular and molecular basis of disease, genetics, and pharmacological sciences. Increasingly, however, the investigations supported by the Institute cut across these program lines. This is particularly true in the fields of structural biology, biotechnology, molecular medicine, and developmental biology.

NIGMS is also the focal point at NIH for activities designed to increase the number of minority biomedical scientists. One such program makes research grant awards to scientists at institutions with substantial minority enrollments. In addition to supporting research studies, these awards help strengthen the overall biomedical research capabilities of the institutions and afford opportunities for students to work as part of a research team. Another program supports biomedical research training for minority students from the undergraduate level through the postdoctoral level.

Complementing these longstanding activities is a new NIGMS initiative, announced in early 1991, that provides predoctoral fellowships to a broader range of outstanding minority students. Over 100 of these fellowships were awarded in September 1991, two-thirds of them funded by NIGMS and one-third funded by other NIH components.

These research and training activities for minority scientists are part of a larger NIGMS effort to provide promising new investigators with the background necessary to build successful research careers. In addition to its traditional training programs, NIGMS has several programs that address special areas of scientific need. These include biotechnology, molecular biophysics (with a focus on the interdisciplinary training needed for research on AIDS), and an integrated curriculum of scientific and medical study leading to the combined M.D.-Ph.D. degree.

Searching for Structures

NIGMS plays a pivotal role in the support of research that determines molecular structures at high resolution. Much of our current understanding of the detailed mechanisms by which biological molecules function has come from application of the techniques of structural biology, such as x-ray crystallography and nuclear magnetic resonance spectroscopy. Among the areas in which particular progress has been made is the determination of structures of proteins such as those that are known to regulate gene activity and those that play roles in intercellular communication.

In each of the past several years, teams of scientists supported by NIGMS to apply the techniques of structural biology to the design of drugs for the treatment of AIDS have made significant new findings. This year, the team led by Dr. David Matthews of Agouron, a California biotechnology company, determined the three-dimensional molecular structure of RNase H, a protein critical to the life cycle of the AIDS virus. Knowledge of this structure will provide a valuable target for the rational design of anti-AIDS drugs.

Another major achievement was made by NIGMS grantee Dr. Susan Taylor and her colleagues at the University of California, San Diego. These scientists have provided the first three-dimensional structure of a protein kinase, one of an important class of enzymes that play roles in growth, neurotransmission, and hormone signaling. This work is expected to have rapid application in basic research on the mechanisms of kinase action, as well as in the development of drugs to treat conditions ranging from cholera to cancer.

Structural studies of a guanine nucleotide binding (G) protein, one of a class of key proteins involved in the cell's response to light, hormones, drugs, neurotransmitters, and other outside signals, are being conducted by NIGMS grantee Dr. Alfred Gilman of the University of Texas Southwestern Medical Center at Dallas. This work complements Dr. Gilman's long-term pharmacological studies of G proteins, and should help scientists understand the exact mechanism by which these proteins exert their varied effects. Other NIGMS-supported scientists are exploring the intriguing connection between G proteins and certain genes involved in the development of cancer.

Clarifying Complexities

It is axiomatic in basic biomedical research that every answer leads to more questions. This is particularly true in the study of DNA, which continues to surprise and fascinate scientists as they learn more about its complex organization and behavior.

One of the most startling events in the history of research on DNA was the discovery of introns, sequences that are removed from the RNA copy of DNA before it is translated into protein. Introns interrupt the coding regions of most genes of higher organisms, breaking the genes into small segments, called exons, which are later spliced together to yield mature RNA.

Several NIGMS grantees have focused on how the cell distinguishes between exons and introns so that it knows which genetic information to retain and which to splice out. This recognition problem is complicated by the fact that, in certain circumstances, exons can be "skipped" to create different messages, and also that exons from one message can be joined to exons from another message to generate further novelty. Dr. Susan Berget of Baylor College of Medicine and Dr. Paula Grabowski of Brown University have independently contributed to a new model for splice recognition that should enhance scientists' understanding of this process, which is critical to normal development, as well as to the genesis of disorders caused by erroneous splice site recognition.

Scientists have also long believed that the copying of DNA into RNA is regulated by proteins. However, research by NIGMS grantee Dr. Karen Sprague of the University of Oregon has revealed that an RNA molecule is involved in this copying process, too. Dr. Sprague and her colleagues, who include an NIGMS trainee, are now working to determine what role the RNA plays, and scientists are once again expanding their view of RNA's many functions.

Surprising findings are by no means limited to the field of genetics. For example, research by Dr. L. Jackson Roberts, an NIGMS-supported pharmacologist at Vanderbilt University, has indicated that anti-inflammatory drugs may work somewhat differently than was previously thought. These drugs are known to prevent the body's synthesis of compounds called prostaglandins, which are associated with the process of inflammation, by inhibiting an enzyme that is necessary for prostaglandin formation. Dr. Roberts discovered an additional, nonenzymatic pathway for prostaglandin synthesis that is not inhibited by anti-inflammatory drugs. This finding is leading scientists to investigate other ways in which aspirin and related anti-inflammatory drugs may act, and may be especially important in the treatment of rheumatoid arthritis.

Another NIGMS grantee, Dr. John Monaco of the Medical College of Virginia, has clarified a previously mysterious immunological process, the display of antigens that trigger a response by the immune system. In order for these antigens to be displayed on the cell surface, small protein fragments must cross intracellular membranes. The process by which the fragments move has been unclear, however, because they lack the special signal sequences thought to be critical to membrane transport. Dr. Monaco's discovery of specific genes involved in the movement of these protein fragments may help explain both individual susceptibility to certain diseases and the development of autoimmune disorders, and may have implications for vaccine development.

Important new results also continue to come from NIGMS support of studies on the basic mechanisms involved in the body's response to trauma and burn injury. Recently, Dr. Charles Rice of the University of Washington has demonstrated that a monoclonal antibody can avert the shock reaction caused by severe blood loss. This antibody prevents white blood cells from clinging to blood vessel walls and releasing toxic substances that damage the vessels and impair organ function. Clinical trials of the antibody are expected to begin in the near future.

Demystifying Development

One of the most fundamental questions in biology is how a single fertilized egg becomes a multicellular organism with varied tissues and organs. Until about 15 years ago, scientists were forced to approach this question by using physical or biochemical means to perturb development in simple model organisms and then observing the results. However, technological advances in molecular biology and genetics have made it possible to investigate problems in developmental biology that were previously unapproachable. The results of these studies promise to improve understanding of normal human development, as well as of cancer and other diseases associated with abnormal development and growth.

NIGMS grantees have made especially rapid progress in understanding the regulation of the cell cycle of growth and division, the control of the formation of body parts in early embryos, and the regulation of cellular differentiation into tissues and organs. Much of this progress has depended upon research in relatively simple model systems, including bacteria, yeast, roundworms, fruit flies, and frogs.

Among the scientists who have recently made major advances in developmental biology is Dr. Douglas Melton of Harvard University. He and his collaborators have found specific chemical substances that induce frog eggs to begin to undergo the changes normal in developing embryos, including the correct organization of body structure and the formation of organs. This research could shed light on the action of substances that control cell differentiation in humans.

Another NIGMS grantee, Dr. Mario Capecchi of the University of Utah School of Medicine, has shown conclusively for the first time that homeobox genes, which have been known to regulate body plan development in fruit flies, also direct early development in mammals.

Structural studies of the protein coded by a fruit fly homeobox gene have revealed important details about how the protein exerts its effect on the developing embryo. NIGMS grantees Dr. Thomas Kornberg of the University of California, San Francisco and Dr. Carl Pabo of the Johns Hopkins University (now at the Massachusetts Institute of Technology) showed how the protein binds to the DNA it regulates, and suggested principles that may account for the exquisite specificity of this binding.

Technological Triumphs

NIGMS grantees are responsible for the development of a number of new technologies that play significant roles in both basic research and biotechnology. One such advance, made by Dr. John Fenn of Yale University, enables researchers to convert biologically important molecules to the gaseous form, a key step in the application of an extremely sensitive analytical tool, mass spectroscopy, to the study of proteins. Called electrospray technology, this process greatly improves the degree of resolution and sensitivity with which proteins and other large molecules can be analyzed.

The usefulness of another research tool, the polymerase chain reaction, in amplifying DNA for basic research and clinical diagnosis led NIGMS grantee Dr. Francis Barany of Cornell University Medical College to develop a different method of making multiple copies of DNA sequences of interest. The new approach, called the ligase chain reaction, is particularly valuable for detecting small changes in DNA sequences, such as those responsible for many inherited disorders. Although this technique is still in the early stages of development, it holds great promise for increasing the accuracy of diagnostic tests for a number of diseases.

Dr. Eva Eicher, an NIGMS grantee at the Jackson Laboratory in Bar Harbor, Maine, has devised a new technique called genome scanning that should speed the search for specific genetic mutations. Until now, when scientists looked for the precise span of DNA responsible for a mutation, they required either "flanking markers," stretches of DNA known to lie on either side of the region containing the gene of interest, or a knowledge of what protein (or other molecule) the gene in question encodes. Genome scanning uses molecular biological techniques to detect large differences, such as duplications or deletions, between target genetic sequences. Once scientists find such a difference, they can determine the location--and ultimately the nature--of the genetic mutation involved.

Program Purpose and Method of Operation

NIGMS places major emphasis on the support of individual, investigator-initiated research grants. It funds a limited number of research centers in selected fields--such as trauma and burn research and the pharmacological sciences (including anesthesiology)--in which the interaction of basic and clinical researchers is critical for rapid scientific progress.

NIGMS also funds key research contracts that provide important resources for basic scientists. In the area of research training, the Institute supports a large portfolio of both individual fellowship awards and institutional training grants. Some of these training programs help meet personnel shortages in rapidly expanding fields of science, such as biotechnology, or promote the access of individuals from minority groups to basic research careers.

Funding for the National Institute of General Medical Sciences during the last 5 years has been as follows:

	Amount	FTE
FY 1988	$640,735,000	158
FY 1989	679,265,000	163
FY 1990	705,870,000	172
FY 1991	757,883,000	183
FY 1992	815,134,000	192

Overall Budget Policy

The NIGMS budget request for FY 1993 continues to emphasize basic biomedical research studies through the support of investigator-initiated research project grants. The budget request is $862,069,000, which represents an increase of 5.76 percent over the FY 1992 estimate. Included in this amount is $17,021,000 for AIDS-related research.

The request will support 814 competing research project grants, as compared to 905 in FY 1992. The average cost of competing research project grants will be $200,779, an increase of approximately 5 percent over the 1992 level. The request will support 2,636 noncompeting research project grants at an average cost of $201,305. This represents a 5.1 percent increase over the 1992 average cost. These increases are consonant with the FY 1993 Biomedical Research and Development Price Index (BRDPI) of 5.1 percent and address the cost containment policies as outlined in the NIH Financial Management Plan implemented in FY 1991.

The budget request will fund the same number of research centers, research career awards, other research projects, trainees, and research and development contracts as in FY 1992. This means that 9 research centers, 20 research career awards, 98 MBRS awards, 36 other research projects, 4,232 trainees, and 6 research and development contracts will be supported.

Included in this request are built-in administrative cost increases for both Intramural Research and Research Management and Support. Furthermore, this request will provide support for 193 full-time equivalents (FTE), an increase of 1 FTE over the FY 1992 level.

National Institute of General Medical Sciences

Cellular and Molecular Basis of Disease

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$209,037,000	$223,476,000	$237,874,000	+$14,398,000

The research supported by the Cellular and Molecular Basis of Diseases (CMBD) Program seeks greater understanding of the structure and function of cells, with the ultimate goal of finding ways to prevent, treat, and cure diseases that result from abnormal cellular activity. Researchers supported by this component of the Institute focus on the molecular and biochemical description and analysis of events in normal and abnormal cells. A broad array of quantitative methods and instrumentation is used in this research, as are techniques of molecular genetics and structural biology.

The CMBD Program supports basic cellular and subcellular research that falls outside the disease-oriented mission of one of the other NIH Institutes, or that examines cellular abnormalities that relate to several diseases or general pathological studies. Research conducted by this Program includes studies of membranes, receptors and signaling, research on cell growth and activation, and investigations of the role and mechanisms of action of enzymes. Other work examines the "machinery" of the cell, its organelles and cytoskeleton.

Rationale for the Budget Request

The FY 1993 budget request for the Cellular and Molecular Basis of Disease Program is $237,874,000, an increase of 6.4 percent over the FY 1992 estimate of $223,476,000. Funding for the Cellular and Molecular Basis of Disease Program over the last 5 years has been as follows:

	Amount
FY 1988	$180,743,000
FY 1989	189,752,000
FY 1990	194,608,000
FY 1991	209,037,000
FY 1992	223,476,000

The following are examples of recent accomplishments of grantees funded by the CMBD Program.

Ligase Chain Reaction

An exciting recent discovery, with significant implications for a number of biotechnology applications, has created competing claims for patent rights. The discovery is a new gene-amplification technique called ligase chain reaction (LCR). It is predicted that LCR will revolutionize DNA diagnostics, just as polymerase chain reaction (PCR) revolutionized basic molecular biology when it was introduced 6 years ago. LCR is similar in many ways to PCR, but differs in ways that may make it important for diagnostic purposes. For example, because of the very high specificity demands of DNA ligases, use of the LCR is much more effective than PCR in recognizing DNA base mismatches. In other words, LCR can spot very slight but important changes in human genes from "standard" sequences.

NIGMS-supported Francis Barany of Cornell University Medical College appears to have been the first to describe in a scientific journal the use of LCR as a genetic screen for a human disease, successfully detecting the tiny mutation that causes sickle cell anemia. Preliminary tests in other laboratories, mostly using Barany's system, seem to confirm LCR's potential. Some scientists are taking advantage of the ease with which different LCR probes can be combined, so that screening for various mutations can be done simultaneously. It is also believed that using PCR's sensitivity and LCR's specificity in tandem may very well prove useful for rapid screening of large populations for disease states.

Aging Proteins can be Repaired by a Common Enzyme

It has been known for some time that proteins spontaneously degrade over time in a wide variety of tissues. Until recently, protein degradation was considered to be a non-specific "scavenging" process. New research has shown that protein degradation is very carefully regulated and, in fact, plays an essential role in cell differentiation and embryonic development. Dr. Vincent Chau of Wayne State University has made excellent progress in determining the molecular details of the process by which mammalian cells degrade proteins. His work promises to contribute significantly to our knowledge of this newly emerging area of cellular control.

Another NIGMS grantee working in this field, Dr. Steven Clarke of the University of California, Los Angeles, has identified several mechanisms of degradation. Specifically, he has determined the role of an enzyme called L-aspartyl/D-aspartyl methyltransferase that repairs proteins by converting their degraded components back to their normal state. This enzyme may be one of a class of enzymes that can check spontaneous protein degradation. An understanding of this process could lead to ways of controlling degradation to preserve cell function and perhaps prevent cell aging, or to speed the degradation of cancerous or other diseased cells.

Protein Identified That Triggers Embryo Formation

In other protein-related studies, Dr. David Melton, an NIGMS supported biochemist at Harvard University, has identified activin as the essential protein that triggers the formation of an animal's most important "core" structural unit--the embryonic head, eyes, backbone, heart and spinal cord. Melton and his colleagues studied fertilized frog eggs that lacked activin, and therefore failed to form the spine-head-heart unit that is the essential core of all animals with backbones. However, when the activin protein was added to the three hour old embryos, the embryos manufactured a rod of cells called the notochord, which allowed development of the vertebral structure, the head, eyes, and associated muscles.

While these experiments were conducted with frog eggs, a similar scenario is believed to occur in humans. Discoveries such as this are expected to lead to an understanding of how embryos normally develop, thus leading to better diagnostic and treatment regimes for a variety of birth defects.

Protein-Lipid Attachments

Another particularly promising area of research has to do with the direct linking of lipids to proteins. It has long been known that some proteins are attached to lipids, the fatty substances that are essential components of all living organisms. However, only recently have the extent, variety, and biological importance of these attachments become of major interest. For example, one type of lipid attachment, called isoprenylation, connects cellular precursors of the lipid cholesterol to a variety of proteins. Several investigators, including NIGMS-supported Dr. Jasper Rine at the University of California, have shown that some cancer-causing oncogene protein products are attached to lipids in this way. The absence of this attached lipid prevents the onset of carcinogenesis caused by the oncogene. This means that scientists can now explore whether therapeutic agents can be developed to keep oncogene products from triggering cancer by devising ways to stop their attachment to lipids.

Mechanisms of Cell Movement

Locomotion of cells is of fundamental importance to biological processes, such as wound healing and inflammation, nerve growth, embryonic development and metastasis of cancer cells. It is hypothesized that determining precisely how a cell makes contact with its external environment will pave the way toward understanding how cells, particularly cancerous cells, invade tissue.

Using "laser tweezers" to stick tiny plastic beads onto living cells, Dr. Michael Sheetz and his colleagues at Duke University, working in conjunction with Dr. Elliot Elson's laboratory at Washington University School of Medicine, reported that a cell's leading edge grabs the surface of an adjacent cell and uses tiny "cytoskeletal motors" to pull itself past its neighbor. After pulling forward, the cell then grows a new leading edge that continues the process. While it was generally accepted that a cell pulls itself forward by grabbing onto a contiguous cell, Dr. Sheetz' work confirmed that the cell's leading edge does much of the work, and that it is structurally and chemically different from the rest of the cell surface.

Understanding how cells move may have important implications in the treatment of infections, other wound-healing processes, halting the spread of cancerous growths, and nerve regeneration.

The Toxicity of Fumonisins

Several discrete toxins, called fumonisins, have been isolated from _Fusarium_, the most prevalent fungi on corn and other grains. Culture materials from this fungus, and from grains that are naturally contaminated with this fungus, have been shown to be toxic and carcinogenic for animals. There is also epidemiological evidence that the fumonisins may cause certain diseases in humans.

While the molecular mechanism of action of the fumonisins is not known, their chemical composition bears a strong structural resemblance to sphinganine, which triggers the biosynthesis of the sphingolipids that play vital roles in various facets of cell growth, cell differentiation, tumor growth, and the functioning of nerve cells. This similarity led Dr. Alfred Merrill and his colleagues at Emory University to propose that the toxic properties of the fumonisins are associated with a disruption of the biosynthetic pathway for sphingolipids.

The potential significance of research on such a natural toxin is considerable, since there are many populations, particularly those in third-world countries, whose daily food consumption consists of large quantities of corn and other grains which may be contaminated with the _Fusarium_ fungus.

National Institute of General Medical Sciences

Genetics

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$214,946,000	$229,530,000	$239,797,000	+$10,267,000

The fundamental studies supported by the Genetics Program continue to yield information vital both to the understanding of many developmental disorders and diseases and to the biotechnology industry. This is because most of the funded research projects are examining the intricate machinery that translates our genetic instructions into the myriad of protein signals that initiate and govern all life processes. Dissecting this machinery into its most basic steps, and determining how and why and in what sequence the steps occur, will ultimately provide scientists with the information necessary to devise the most targeted and effective ways to prevent, diagnose and treat a large number of disorders and diseases. At the same time, while conducting their research, investigators supported by the Genetics Program often develop new techniques and new models for studying human disease that prove useful across many fields of biomedical inquiry, as well as in industry and medical practice.

Rationale for the Budget Request

The FY 1993 budget request for the Genetics Program is $239,797,000, an increase of 4.5 percent over the FY 1992 estimate of $229,530,000. Funding for the Genetics Program during the last 5 years has been as follows:

	Amount
FY 1988	$194,370,000
FY 1989	205,051,000
FY 1990	203,045,000
FY 1991	214,946,000
FY 1992	229,530,000

The following are examples of recent accomplishments of grantees funded by the Genetics Program.

Mouse Models of Human Disease

In recent years, research supported by the Genetics Program has demonstrated the striking similarity across species of the genetic makeup of organisms. Thus, many scientists are now manipulating the genetics of mice in order to answer detailed questions about human embryonic development. During the past year, notable achievements in such mouse models by two NIGMS grantees offer scientists the opportunity to examine the genetic pathways that may account for several human disorders. Dr. Kiran Chada of the University of Medicine and Dentistry of New Jersey has used a technique called "insertional mutagenesis" to isolate two potentially important genes in mice. One gene produces mice that are correctly proportioned but that are about one-third the size of normal mice. In these mutant mice, the circulating level of growth hormone is normal. Furthermore, genetic and molecular studies have shown that the mutant gene is probably the one associated with a line of pygmy mice that arose spontaneously many years ago. This means that Dr. Chada's mouse model can be used to try to identify the comparable human gene and to determine whether the pygmy mouse can serve as an authentic model for human "non-growth hormone deficient dwarf syndrome." Interestingly, since African pygmies, like these mice, have normal levels of growth hormones, studies of this mouse might help scientists understand what determines body size. A second mouse mutant gene discovered in Dr. Chada's laboratory may serve as a model for certain defects that account for human infertility, particularly the human disease known as premature ovarian failure.

Another grantee, Dr. Mario Capecchi of the University of Utah School of Medicine, used another method, known as "gene targeting," to create a mouse model in which one of the so-called homeobox genes, genes known to play a central role in proper development of segments of the body plan, has been disrupted. The mouse progeny exhibited developmental abnormalities that bear a striking resemblance to the abnormalities of the life-threatening human congenital disorder, DiGeorge syndrome. Dr. Capecchi's work in vertebrates also confirms that the homeobox genes, most thoroughly studied in fruit flies, are indeed important regulators of development in higher organisms, including man. His findings are likely to be only the first of a series of discoveries about the precise function of each of the 40 or so homeobox genes in mice, each of which almost certainly has a human analog.

Fruit Fly Model for Targeted Gene Replacement

Gene targeting, in which a naturally occurring gene is replaced with an artificially altered copy, has become a powerful tool for studying the function and expression of genes. To be successful, gene targeting requires a method for insuring that the added DNA will be integrated into the genome at its normal chromosomal location. Until now, this precise integration has proven almost impossible to achieve in the much-studied fruit fly; instead, scientists have had to be content with random insertions of new DNA. A breakthrough has recently been reported by Dr. William Engels at the University of Wisconsin. He has used properties associated with the presence of a particular genetic element, called a "jumping gene," within or near a target gene of interest. When one of these elements "jumps" out of its normal location, it leaves a gap. Then, the genetic material searches for an identical replacement to "fill in the gap" and to repair itself. This process creates the opportunity for scientists to incorporate an altered gene at the precise location from which the jumping element moved. This is the first time that targeted gene replacement has been possible in fruit flies, and may point the way to the future development of similar techniques in other organisms, which might serve as useful models for human diseases.

Genetic Control of the Cell Cycle in Yeast

Although the cell division cycle proceeds through four clearly separable phases--that preceding DNA replication, DNA synthesis itself, a pause after DNA replication, and then mitosis (cell division), in reality, a much larger number of cell processes are involved in the cell division cycle and these must be elaborately orchestrated for normal division to occur. Recent studies by a number of NIGMS grantees have demonstrated the existence of so-called "checkpoint" genes. Their function is to prevent the cell cycle from proceeding until earlier events have been satisfactorily completed. Drs. Leland Hartwell and Ted Weinert at the University of Washington have identified in yeast a "checkpoint" gene, labeled RAD9, that appears to be part of a feedback system that prevents the cell from proceeding to mitosis if too many copies of unreplicated DNA exist in the cell. Grantees of the Genetics Program in other laboratories have discovered additional factors that exert similar effects in developing fertilized frog eggs. Together these discoveries suggest that improperly functioning "checkpoint" genes may contribute to birth defects and to the uncontrolled division of cells that occurs in cancer.

Fluorescent Labeling of Genes and Chromosomes

Dr. David Ward of Yale University has made stunning progress in applying to new research problems a technique which he developed two years ago, called high resolution chromosome fluorescence in situ hybridization. At first, Dr. Ward had used fluorescent labeling to permit him to easily map fluorescently-tagged genes to precise locations on specific chromosomes, work he is still continuing as part of the Human Genome Project. However, he can now apply his fluorescence technique to visualize many different forms of DNA simultaneously in the same cell, or to "paint" whole chromosomes with different fluorescent tags. These advances permit him to more easily detect chromosomal abnormalities, such as the extra copy of chromosome 21 that signals Down Syndrome or the translocation of a piece of one particular chromosome to another chromosomal location. Another application of this technique is in tumor identification. Determination of tumor types is facilitated by examination of the kinds of chromosomal abnormalities that the cancer has caused. Being able to "paint" specific chromosomes simultaneously with different fluorescent tags will speed this process and improve its accuracy. In addition, this fluorescent labeling can be applied to a study of the extent of integration of the DNA of an infecting virus into the DNA of particular host cells, and to a determination of which tissues in the body the virus has invaded.

The Role of Histones in Gene Expression

For the past 15 years, many grantees of the Genetics Program have been intent on discovering how transcription occurs--that is, what the steps are by which genetic information is copied from the DNA code into the RNA, which, in turn, provides the cell with the instructions for making proteins. This process is central to life and health. Identification of the factors that trigger transcription is of enormous importance. Studies of transcription factors have been done, for the most part, in the test tube using so-called "naked DNA," which is not the natural state of this nucleic acid. Recently, however, it has become clear that in nature, where DNA inside cells is tightly coiled around and compacted by histones (a specialized set of proteins), transcription proceeds in a more complicated fashion, making it more difficult to study than in the test tube. Dr. Michael Grunstein of the University of California at Los Angeles and Dr. James Kadonaga of the University of California at San Diego have shown that histones, which were previously thought to serve only a structural role, also play a central role in regulating gene expression. Dr. Grunstein has demonstrated that the H4 histone, around which DNA coils, contains a region that must be present for normal transcription to occur. Presumably, this region of the H4 histone facilitates the uncoiling of the DNA from around the histones, allowing the transcription factors to bind to the DNA. Dr. Kadonaga has found that another histone, H1, known to have a unique structural role among the histones in compacting the coils of DNA, normally represses transcription. However, in combination with other specific transcription factors, it acts to enhance transcription in a gene-specific manner. Clearly the entire process of transcription is extremely complex and results from the interplay of a number of proteins, including both transcription factors and histones. The work of Drs. Grunstein and Kadonaga is likely to spur renewed interest in the role of histones in regulating gene expression, a role which has been neglected for many years.

National Institute of General Medical Sciences

Pharmacological Sciences Program

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$108,764,000	$122,066,000	$129,927,000	+$7,861,000

The Pharmacological Sciences (PS) Program supports a broad spectrum of research aimed at improving our understanding of the biological phenomena and related chemical and molecular processes involved in the actions of therapeutic drugs and of the biological breakdown of the products that the body produces from these drugs. The scope of the PS research program extends from synthetic chemistry and basic biological and biochemical studies related to molecular pharmacology and anesthesiology to controlled clinical investigations of pharmacological agents in patients and normal volunteers.

Rationale for the Budget Request

The FY 1993 budget request for the Pharmacological Sciences Program is $129,927,000, an increase of 6.4 percent over the FY 1992 estimate of $122,066,000. Funding for the Pharmacological Sciences Program during the last 5 years has been as follows:

	Amount
FY 1988	$88,124,000
FY 1989	92,519,000
FY 1990	97,332,000
FY 1991	108,764,000
FY 1992	122,066,000

The following are examples of recent accomplishments of grantees funded by the Pharmacological Sciences Program.

G Proteins

Understanding the role that proteins play in maintaining health and disease is a crucial first step in devising therapies for a variety of diseases that range from asthma to various endocrine disorders such as pituitary tumors. The study of the structure, function, and regulation of proteins, both normal and abnormal, is therefore one of the most active fields in pharmacology and other areas of basic research. One area yielding particularly intriguing results is the study of the guanine nucleotide binding proteins, or G proteins, which are involved in such diverse activities as the response of the eye to light, the development of pituitary tumors, neurotransmission, the learning process, and the adverse effects of cholera and whooping cough.

Dr. Alfred Gilman, a former NIGMS Pharmacology Research Associate and a current NIGMS grantee at the University of Texas Health Science Center at Dallas, has recently crystallized the G protein subunit most critical to its activity, paving the way for 3-dimensional structural studies. This work should help scientists understand the exact mechanism by which G proteins exert their varied effects, and should shed light on the connection between G proteins and genes involved in the development of cancer.

Immune System Protein Studies Yield Hope for Transplant Patients

Dr. Stuart Schreiber at the Chemistry Department at Harvard University has investigated the chemistry of immunosuppressive agents, which are drugs used to prevent rejection of transplanted organs. His efforts demonstrate the ability of chemists to effectively address biological problems.

One important type of cell in the immune system, the so called T-cells, contain a class of proteins called "immunophilins," which were initially identified because they are the receptors in the cell for immunosuppressive drugs. The most commonly used immunosuppresive drug has been cyclosporine. However, it has many side effects, such as hypertension and kidney damage. In the late 1980s, two new immunosuppressant agents, FK506 and rapamycin, were discovered. Both have been shown to be much more powerful and to have less toxicity than cyclosporine. In an attempt to better understand how these drugs act and further improve their efficacy in organ transplantation, Dr. Schreiber and Dr. Nolan Sigal of Merck Sharpe and Dohme, 2 years ago, each independently identified the receptor immunophilin, FKBP, to which both rapamycin and FK506 bind.

This year Dr. Schreiber and his colleagues at Harvard deciphered the atom-by-atom structure of FKBP, and determined the process by which it interacts with FK506. It appears that the process of binding to that common receptor leads to immunosuppression in a different way for these two drugs. This distinction holds great promise for the treatment of transplant rejection, because it means that using FK506 and rapamycin together could be more effective than using either one alone.

A few world-class chemists, like Dr. Schreiber, have begun to work in an area of science that combines the specialized fields of chemistry and biology, referred to as the chemistry-biology interface. But few biologists or chemists today have received the truly multidisciplinary training that both academicians and industry leaders insist is needed in order to capitalize on the areas of opportunity that are ripe for exploitation, particularly in the fields of biotechnology and pharmaceuticals. This multidisciplinary approach, i.e., chemists who understand biology, and vice versa, is necessary to bridge the boundary between chemistry and biology. The Institute is currently evaluating the feasibility of establishing a new training grant initiative that addresses this shortage.

Prostaglandins

Another important field of pharmacology research is typified by the NIGMS-supported work being conducted by Dr. L. Jackson Roberts at Vanderbilt University. Dr. Roberts' research has shown that patients with mastocytosis, a rare but potentially fatal disorder, secrete large amounts of a chemical called prostaglandin D2 in their urine. This substance is responsible for blood vessel dilation leading to intense flushing and often to a critical drop in blood pressure. Last year, Dr. Roberts reported that patients with this disorder, as well as those taking niacin for high cholesterol levels, which also leads to intense flushing, are often successfully treated with aspirin. This common drug interferes with the synthesis of prostaglandins by inhibiting an enzyme that is necessary to their formation.

This year, further studies on prostaglandins by Dr. Roberts indicate that, in addition to being synthesized by pathways sensitive to aspirin, these same prostaglandins also are made in large amounts by a non-enzymatic pathway that is not inhibited by aspirin. This discovery has challenged current scientific dogma regarding the mechanism by which aspirin helps in the treatment of rheumatoid arthritis, a disease from which more than two million Americans suffer. By helping to define the exact substance involved in joint inflammation in rheumatoid arthritis, Dr. Roberts' work should point the way to more effective treatment, thus paving the way for increased productivity and improved quality of life for the many people afflicted with this disease.

Anesthesiology

Anyone undergoing surgery is likely to receive some form of general anesthetic. While the relative safety of this class of drugs is acknowledged, virtually all people suffer some degree of unpleasant side effects. Occasionally, more serious adverse reactions occur in individuals who, when exposed to certain anesthetic agents, are genetically predisposed to developing a potentially lethal hypermetabolic state called "malignant hyperthermia." Several new investigators, who are products of NIGMS-supported postdoctoral research training programs in anesthesia research, are trying to characterize the mechanism of anesthetic action at the molecular level. These include Dr. Margaret Sedensky at Case Western Reserve University, and Dr. Alex Evers at Washington University. Initial findings indicate that particular general anesthetics do indeed have specific molecular sites of action, and that scientists are on the threshold of positively identifying the site(s) at which these agents act. Their work is expected to provide the necessary information for the development of safer and more effective anesthetics, as well as for a non-invasive diagnostic procedure that could predict serious adverse reactions, such as malignant hyperthermia, in susceptible individuals.

Another NIGMS grantee at Vanderbilt University, Dr. Grant Wilkinson, is examining how individuals, including persons from diverse ethnic populations, differ in their ability to metabolize drugs due to variations in the levels and activity of enzymes responsible for drug metabolism. Recent work by Dr. Wilkinson and his colleagues, one of the few groups working in this area, has shown that 3 to 5 percent of Caucasians are poor metabolizers of the anticonvulsant drug, mephenytoin, while that percentage is 5 to 6 times higher in Japanese populations and drops to zero in the Cuna Amerindians of Panama.

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In examining the variations in metabolism of the commonly used drug, codeine, Dr. Wilkinson has found that approximately 8 percent of Caucasians are poor metabolizers. Since it is the metabolized product of codeine that provides its analgesic effect, poor metabolizers essentially receive no analgesic effect after taking codeine. Following up on these population variations in the ability to metabolize drugs should rapidly lead to improved drug therapy for severe pain.

National Institute of General Medical Sciences

Biophysics and Physiological Sciences

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$155,111,000	$164,076,000	$177,095,000	+$13,019,000

The research funded by the Biophysics and Physiological Sciences (BPS) Program brings the tools of many disciplines to bear on studies ranging from basic structural biology to clinical investigations regarding the treatment of trauma. Molecular genetics, sophisticated x-ray crystallography and nuclear magnetic resonance imaging, chemistry, mathematics and engineering are used in combination to solve fundamental biomedical problems of interest to the research enterprise, to health care providers, and to the biotechnology industry. For example, many scientists supported by the BPS Program are studying proteins and nucleic acids at the level of the atoms that determine their molecular design. These studies are critical not only to an understanding of their function but also to the rational design of new therapeutic agents. Investigators examining the body's response to trauma are using biochemical and molecular genetics to understand, at the molecular level, many of the cascading physiological perturbations that follow trauma or burn injury. This work is beginning to serve as the basis for the design of new therapies for the traumatized patient.

Rationale for the Budget Request

The FY 1993 budget request for the Biophysics and Physiological Sciences Program is $177,095,000, an increase of 7.9 percent over the FY 1992 estimate of $164,076,000. Funding for the Biophysics and Physiological Sciences Program over the last 5 years has been as follows:

	Amount
FY 1988	$121,822,000
FY 1989	133,376,000
FY 1990	146,954,000
FY 1991	155,111,000
FY 1992	164,076,000

The following are examples of recent accomplishments of grantees funded by the BPS Program.

Defining the Structure of an AIDS Virus Protein

Over the past 10 years, scientists, using bacteria and other model systems, have determined that several classes of proteins regulate the transcription of RNA, the first step in gene expression. Recently, grantees of the BPS Program have turned their attention to the proteins that control the expression of genes in higher organisms, including man. One group of such proteins share a common sequence pattern of amino acids (the "building blocks" of proteins) and bind to DNA only when attached to zinc ions. These stretches of transcriptional proteins have been termed "zinc fingers" and appear to share a common structure. In the past few years, Dr. Michael Summers at the University of Maryland has focussed his studies on the nucleocapsid protein that encapsulates the HIV-1 virus that causes AIDS. This protein, common to a number of retroviruses like HIV-1, contains two stretches of "zinc finger" sequences at which binding to RNA, a step vital to infectivity, is thought to occur. Dr. Summers has used nuclear magnetic resonance spectroscopy to determine the unique structure shared by these two retroviral-type "zinc finger" stretches of protein. The structure he has proposed seems consistent with the biological activity of the molecule and now that the structure of this vital protein region has been elucidated, further studies can proceed, in hopes of determining new treatments for or vaccines against the HIV virus. For example, it might be possible to design compounds based on the premise that interfering with the zinc binding of the HIV retroviral proteins will interfere with, or prevent progression of viral infection.

Structure Determination of the Homeodomain

Geneticists who are trying to understand how genes control early development, particularly how they signal the formation of the different tissues that comprise the various regions of the organism, are concentrating their efforts on determining the role of the so-called homeobox genes. The homeobox is a highly conserved stretch of genomic DNA that has been shown to be involved in pattern formation in organisms as diverse as the fruit fly and man. The homeobox genes code for homeodomains, that is, portions of proteins that regulate the transcription and expression of the genes by binding to specific promoter regions. The homeodomains of different proteins, though structurally similar, clearly must bind to different points along the genetic material in order to regulate different aspects of pattern formation during development. To account for such differences in binding, scientists have been eager to examine in detail the binding of the homeodomain to DNA. Recently, a BPS-supported grantee, Dr. Carl Pabo, then at Johns Hopkins University, collaborated with Dr. Thomas Kornberg at the University of California, San Francisco, a grantee of the Genetics Program, using X-ray crystallography to determine the structure of the homeodomain-DNA complex. The details of the structure they found suggest that the highly conserved portion of the homeodomain forms an important core recognition site for binding with DNA, but that subtle differences within that core must determine to which genes these transcription factors bind and at what specific times during development. Thus, as is often true in research, Dr. Pabo's structural work, while answering some key questions, has raised others that will require further study.

Structural Studies of Protein Kinases

For some time, scientists have known that enzymes called protein kinases are important intermediaries in many pathways by which hormones, growth factors, neurotransmitters, and toxins exert their effects. Several protein kinases are also known to transmit growth signals that can, if defective, trigger the growth of malignant tumors. Recently, Dr. Susan Taylor of the University of California, San Diego, became the first to determine the sequence and the three-dimensional structure of a particularly important protein kinase, the cyclic-amp dependent protein kinase. At the heart of the enzyme is a "core" sequence and structure shared by all known protein kinases found in higher organisms. This discovery of the structure of a particular kinase lays essential groundwork for understanding the mechanisms of action of this entire class of enzymes. The exciting next step is to take advantage of the molecule's structural conformation as the basis for the rational design of anticancer and other drugs.

Cryopreservation of Organs

It is almost a truism of biology that man must struggle to achieve what nature seems to do so simply. Thus, while scientists have, for years, tried to find ways to freeze and thaw organs (e.g., hearts and kidneys destined for transplantation), some simple vertebrates, like frogs, hibernate and undergo freeze-thaw cycles without injury. In recent years, cryopreservation has become an important tool for modern medical science in that a variety of single cells, such as blood and bone marrow, as well as simple tissues, such as cornea and skin, can be stored for long periods of time at deep subzero temperatures with successful resumption of function after thawing and transplantation. The increasing use of organ transplant therapy is now fueling the drive to extend preservation by freezing to intact organs, in order to extend their viability in "organ banks." Dr. Kenneth Storey, an NIGMS-supported granteee at Carleton University in Ottawa, Canada, has taken advantage of the unique natural freeze tolerance of hibernating frogs to study organ-specific cryopreservation. He has discovered the factors in these frogs that account for their survival during freezing and through the thawing period. These include: the particular proteins in their blood that control the rate of ice formation during freezing, one key to preventing damage to the tissues; other cryoprotectant substances that protect and stabilize cell membrane structure and hold ice-formation at tolerable levels; and mechanisms to adjust their metabolic rate to a tiny fraction of normal and to generate energy in the absence of oxygen. These findings are now serving as the basis for studies to search for synthetic equivalents of the frogs' protective proteins and for ways to develop strategies for metabolic arrest that might be useful for human organ cryopreservaton.

Wound Healing

A number of BPS-supported scientists are investigating the effects of topical growth factors on repair of wounds caused by burns, surgery, and both major and minor trauma. Investigators at Vanderbilt University have reported that wound healing can be accelerated by the topical application of epidermal growth factor, EGF. Other clinical studies at the Brigham and Women's and Beth Israel Hospitals in Boston, and at the University of Texas Medical School at Galveston, have shown that the administration of human growth hormone not only accelerates the rate of wound healing, but also preserves total body muscle strength and function. The use of this treatment can substantially reduce the rehabilitation time required for severely traumatized and burn patients. For example, in badly burned children to whom human growth factor had been administered, hospital stays were reduced by an average of 20 days.

National Institute of General Medical Sciences

Minority Opportunities in Research Programs

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$46,226,000	$47,671,000	$47,671,000	---

	FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
Minority Opportunities in Research:				
Minority Biomedical Research Support Program	$31,614,000	$33,059,000	$33,059,000	---
Minority Access to Research Careers Program	13,220,000	13,220,000	13,220,000	---
Special minority initiatives	1,392,000	1,392,000	1,392,000	---
Total	46,226,000	47,671,000	47,671,000	---

In 1991, the National Institute of General Medical Sciences established the Minority Opportunities in Research (MORE) Programs Branch to serve as the administrative umbrella for both the Institute's existing programs and its new efforts aimed at increasing the number of underrepresented minorities engaged in biomedical research. The Branch is the focus of planning and coordination of the activities of the Minority Biomedical Research Support (MBRS) Program and the Minority Access to Research Careers (MARC) Program, as well as of special initiatives, including the new national predoctoral fellowship program. The leadership and administrative oversight provided by this new Branch should enhance the success of the existing programs and open new opportunities for expanding the participation of minorities and minority institutions in sponsored research and in developing the pipeline for new research scientists.

The MORE Programs Branch is responsible for planning the Institute's meetings and other activities which build networks among individuals, institutions and others who share an interest in increased participation of minorities in research. One featured meeting is the Minority Programs Symposium, most recently held in November 1991, at which participants in the MBRS and MARC Programs gather to make scientific presentations and to learn of opportunities for research experiences and graduate education. In addition, the branch hosts both formal and informal meetings designed to explain all of the Institute's programs and to facilitate participation in, or partnership with, those programs. A series of regional workshops with institutions not currently participating in either the MBRS or MARC Programs will continue into FY 1993. These workshops should enhance the dialogue between these academic institutions and Institute staff and should lay the groundwork for constructive relationships.

Rationale for the Budget Request

The FY 1993 budget request for the Minority Opportunities in Research Programs branch is $47,671,000, the same level as in FY 1992. Funding for the Branch's programs over the last 5 years has been as follows:

	MBRS	MARC	Special Initiatives	Total MORE
FY 1988	$28,342,000	$8,709,000	---	$37,051,000
FY 1989	28,147,000	9,053,000	---	37,200,000
FY 1990	29,794,000	10,670,000	---	40,464,000
FY 1991	31,614,000	13,220,000	$1,392,000	46,226,000
FY 1992	33,059,000	13,220,000	1,392,000	47,671,000

Descriptions of the scope and accomplishments of the branch's various programs follow.

Minority Biomedical Research Support Program

The MBRS Program awards grants to educational institutions with substantial minority enrollments to support research by faculty members, to strengthen the schools' overall biomedical research capabilities, and to provide opportunities for students to work as part of a research team. Awards are also made to permit enrichment activities, such as enhanced science curricula, and attendance by faculty and students at scientific meetings and participation in research during the summer at off-campus laboratories. Faculty members who receive MBRS support are expected to submit their results for publication in peer-reviewed scientific journals, to make presentations of their research at scientific meetings, and to develop research projects to the point of trying to obtain other support for their research.

Typically, 95-100 institutions receive grant support from the MBRS Program. Of the 96 institutions receiving awards in FY 1991, 53 primarily serve Black Americans, 5 primarily serve Native Americans, 8 primarily serve Puerto Ricans, 11 primarily serve other Hispanic Americans, and 3 primarily serve Asians or Pacific Islanders. The remaining awards were made to institutions with large, mixed populations of minority students. The funds provided support for the research efforts of 739 faculty members working on 630 research projects. A total of 1,034 undergraduate and 425 graduate students participated in these projects as research assistants. Since the program's inception in 1972, approximately 16,500 students have held such positions on MBRS-supported projects.

Recognizing that it is important to tailor grant programs to maximize their utility to particular types of educational institutions, the MBRS Program relies on two grant mechanisms. One of these, the MBRS Traditional Program, is used most often and provides funds to schools that already have both research capabilities and comprehensive science programs. These awards typically support faculty research projects that involve substantial student participation. In a few schools which have substantial minority enrollments, support is limited to student participation on research projects which are funded by other, non-MBRS sources. In both of these cases, students learn research techniques and practice scientific methods by participating in research projects already under way at their own academic institutions.

A second funding mechanism is the MBRS Program for Undergraduate Colleges. These awards largely support science and research-related enrichment programs for students and faculty at institutions with limited science programs. Activities include workshops, attendance at scientific meetings, and summer research experiences, most often at laboratories at other universities, in industry, or in government. On occasion, pilot and ongoing research projects performed by faculty members are also supported.

The impact of these MBRS programs on the institutions, as well as on the faculty and students involved, is significant. Many institutions have developed a research infrastructure and enhanced their science curricula in order to be competitive in the MBRS Program and to attract and retain high-caliber faculty and students. In addition, reports received from institutions that have participated in the MBRS Program for many years have included numerous examples of students whose experiences have launched them into advanced biomedical research training and then into biomedical research careers. Currently available information on student participants in the MBRS program shows that 1,304 students have completed the M.S. degree, 415 have completed the Ph.D. degree, 770 have obtained the M.D. degree and 123 have obtained the D.D.S. degree. These data have been matched with the Doctorate Record File, compiled by the National Research Council.

Minority Access to Research Careers Program

Sparked by efforts to help reduce the projected shortfall of research scientists and responding to an increasing demand for minority scientists by academic institutions, industry, and the government, the Minority Access to Careers (MARC) Program was formally established in 1972. The MARC Program supports biomedical research training for students and faculty members primarily at four-year colleges and universities which have substantial minority enrollments. By enabling grantee institutions to develop and enhance their biomedical research training opportunities and capabilities through strengthening science curricula, offering seminars, and off-campus research activities, a significant number of students graduate with a commitment to pursue further a biomedical research career through graduate school. Since its formation, the MARC Program has demonstrated a continual record of success by supporting approximately 2,700 students, with 80 percent of its students continuing their education in professional or graduate school--in comparison to the national average of less than 20 percent of minority science majors who do so. Preliminary data also suggests that three quarters of those MARC students who begin a graduate program go on to complete it, with 60 percent of that number earning Ph.D.s and the remainder achieving medical degrees.

In order to pursue its objectives, the MARC Program administers individual and institutional research training grants. Established in 1977, the Honors Undergraduate Research Training (HURT) grants focus on stimulating the most capable students to continue their studies in biomedical research into graduate school and an eventual scientific career. Through the grantee institutions, MARC HURT trainees receive hands-on research experience, rigorous instruction in the sciences fundamental to biomedicine, and mentoring relationships with biomedical sciences faculty. Students participating in this program are required to have at least one off-campus summer research experience, for example, in a research laboratory in another academic institution, government laboratory, or in industry. Together, these experiences involve students in the excitement of science and improve their ability to compete for entry into high-quality graduate training programs. By far the largest program component, the Honors Undergraduate Program activities amounted to just under 75 percent of the MARC Program funds, or $10.9 million, in FY 1991. Sixty-two minority institutions received support for these special programs for junior and senior honors students. In 1991, the Honors Undergraduate Research Training Program expanded its eligibility to freshman and sophomore level undergraduates with the goal of instilling and sustaining scientific interest in students at a critical and formative point in their college careers. Fifteen schools received awards for this pilot program.

As a further incentive for graduates of the Honors program to continue their studies, the MARC Predoctoral Fellowship Awards provide successful applicants with financial support to pursue graduate studies leading to the Ph.D. or combined M.D.-Ph.D. degree in the biomedical sciences. Fellowship support includes tuition, a stipend, and funds to help defray the cost of laboratory supplies and to permit limited travel. To date, 171 fellowships have been awarded, with 30 being made in FY 1991.

Another MARC fellowship program is designed to assist faculty members aspiring to acquire advanced graduate degrees or to do postdoctoral research in prominent universities and laboratories external to their home institutions. These MARC Faculty Fellowships provide financial support to selected full-time faculty members of 4-year colleges, universities, and health professional schools with substantial minority enrollments. Since its inception in 1972, 232 individuals have received support under this program; 4 were awarded in FY 1991. Of those who have completed the training period, approximately 90 percent have returned either to their original home institution or to another minority institution.

Finally, the MARC Visiting Scientists Awards allow exceptional scientist-teachers to serve as visiting scientists at colleges and universities with significant minority student enrollment. Scientists share their special talents, including innovative and state-of-the-art research techniques, with both students and faculty. In recent years, NIGMS has funded this effort through the Federation of American Societies for Experimental Biology (FASEB) for its Visiting Scientist for Minority Institutions Program.

Other Special Initiatives

In response to Congressional interest, NIGMS initiated a program of national predoctoral fellowship awards for minority students in February 1991. Eligibility for these graduate fellowships is open to minority graduates of any college or university, including the many minority undergraduate students who have participated in NIH-sponsored programs or the National Science Foundation programs. Similar in concept to the Minority Access to Research Careers predoctoral fellowships, this support mechanism permits the pursuit of a research doctorate (a Ph.D. or M.D.-Ph.D.) to be financially viable for many more minority students. These fellowships provide a stipend plus tuition, fees, and a small allowance for supplies and travel for up to five years. In FY 1991, NIGMS made 65 awards under this program, while another 36 awards were funded by the Office of Minority Programs, NIH, and several other NIH components. A number of NIH components have agreed to join in the reannouncement of these fellowships in FY 1992 for future awards.

Success of Programs

The positive impact of the MARC and MBRS programs is best illustrated by the individuals described below:

° Dr. Charles Richard Neal, Jr., a scientist who has received support through both the MBRS and MARC Programs, was the 1991 recipient of the University of Michigan's Medical Scientist Training Program (MSTP) Award. The award was established in 1984 to honor one graduating MSTP student who demonstrates outstanding accomplishments in research and who also exhibits the personal and professional qualities desired in a physician. A New Mexico native, Dr. Neal attended the University of California, Santa Cruz, where he participated first in the MBRS Program and later in the MARC Program. In 1984, with support from a MARC predoctoral fellowship, Dr. Neal enrolled in the University of Michigan MSTP and began his studies toward the combined M.D.-Ph.D. degree.

° Dr. Georgina Hart, an MBRS graduate of Inter American University of Puerto Rico in Hato Rey, was the first alumna to receive a Ph.D. in chemistry. After receiving her doctorate from the University of Miami in Florida, Dr. Hart became an associate professor at Inter American. She is now engaged in industrial research.

° Dr. Cynthia Burroughs was a MARC graduate of Talladega College in May 1983. Her subsequent graduate work in biochemistry at the University of California at Berkeley was supported through a MARC predoctoral fellowship. Dr. Burroughs spent two years as a postdoctoral fellow at the National Institute of Environmental Health Sciences, NIH, in North Carolina, before becoming an Assistant Professor of Biochemistry at the University of California, Hayward.

National Institute of General Medical Sciences

Intramural Research

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
18	$1,082,000	22	$1,237,000	22	$1,300,000	---	+$63,000

The NIGMS has a small, but unique, intramural research program, formally known as the Pharmacology Research Associate (PRAT) Program. Under its auspices, a group of recently trained scientists is selected each year for a 2-year period of postdoctoral research experience under the direction of preceptors in the intramural laboratories of the various categorical institutes of the National Institutes of Health (NIH) and the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA). The goal of this program is to develop topflight leaders in pharmacological research who will take key positions in academic, industrial, and government research laboratories. The program is intended for those who have made a commitment to pharmacology through their previous training or research activities, and for those with backgrounds in clinical medicine or other biological sciences who wish to acquire specialized experience in the field of pharmacology. The individuals chosen for this program are selected on the basis of their academic records, demonstrated research interest, and research accomplishments. They receive high-quality postdoctoral research experience working with any of over 120 senior scientists, including Nobel Prize winner Dr. Marshall Nirenberg and Dr. French Anderson, a pioneer in the basic science supporting gene therapy. In addition, they may take coursework in such areas as pharmacokinetics, experimental statistics, medicinal chemistry, biochemical genetics, and molecular biophysics.

Rationale for the Budget Request

The FY 1993 budget request for the NIGMS Intramural Research Program is $1,300,000 an increase of $63,000 over the FY 1992 estimate. Funding for the Intramural Research Program during the last 5 years has been as follows:

	Amount	FTE
FY 1988	$788,000	17
FY 1989	951,000	18
FY 1990	1,072,000	20
FY 1991	1,082,000	18
FY 1992	1,237,000	22

This request will provide support for a total of up to 22 PRAT fellows. It is the intent of the Institute to keep this a small program, but one of the highest quality.

Profile of PRAT Program Participants

Since its establishment in 1965, 251 scientists have graduated from the PRAT Program. It is known that at least 226 (90 percent) of them have entered research careers. Of these, 109 are located at academic or independent research institutions, 83 at NIH or other Federal research facilities, and 36 at various pharmaceutical firms. Almost 40 percent of the PRAT graduates who are engaged in research possess an M.D. degree, indicating that the program has succeeded in attracting and directing a large number of physicians into research careers instead of into clinical practice.

Since 1978, the PRAT Program has made several positions available that are specifically targeted to research in clinical pharmacology. Applicants for such positions must have the M.D. degree, a minimum of 1 year of graduate medical training (internship or residency), and a demonstrated interest in a research career in clinical pharmacology. This sub-program offers qualified candidates opportunities for training in research directly related to the clinical use of drugs such as the distribution, mode of action, metabolism, and excretion of drugs in the human body. It is designed to attract more physicians into what is considered to be a shortage area by the Forum on Drug Development and Regulation of the Institute of Medicine.

Notable PRAT Fellow Accomplishments

The PRAT Program is widely recognized for its excellence. Fellows in the program have the opportunity to pursue research in some of the most exciting areas of the pharmacological sciences and related fields. For example, Dr. Andrew Shenker, a PRAT fellow from 1989 to 1991 in the laboratory of Dr. Allen Spiegel of the National Institute of Diabetes and Digestive and Kidney Diseases, recently discovered that blood platelets contain a novel type of guanine nucleotide binding protein, or G protein. G proteins play a critical role in the transmission of signals received through cell membranes in species ranging from roundworms to humans, and are implicated in an ever-widening array of biological processes, including smell, vision, memory, development, neurotransmission, and a variety of diseases such as cholera, whooping cough, and arthritis, as well as in the development of tumors. Dr. Shenker has provided important new information about G proteins and their roles in cell function. His work moves researchers a step closer to finding ways to treat conditions resulting from faulty G protein function.

National Institute of General Medical Sciences

Research Management and Support

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
165	$22,717,000	170	$27,078,000	171	$28,405,000	+1	+$1,327,000

The Research Management and Support budget provides funds for salaries, equipment, supplies, and other administrative costs required to support the Institute's extramural staff. The Office of the Director continues to sustain a leadership role by directing, advising, and overseeing the many diverse program areas within the Institute. By maintaining contact with the scientific and academic community, this Office is perpetually conscious of the public's major health and research concerns. The Office of the Director utilizes this information to evaluate current research topics, and select promising areas of research for new or expanded investigation. The vast majority of the Institute's overhead resources is devoted to the functions of scientific review, the scientific administration of grants and contracts, and the fiscal stewardship function that accompanies a sizable extramural program supporting research and research training in the biomedical sciences.

In addition, the Research Management and Support budget funds: (1) services provided centrally by NIH organizational units which do not receive direct appropriations, such as the Division of Research Grants (DRG); (2) program evaluation studies; and (3) the National Advisory General Medical Sciences Council (NAGMSC).

Rationale for the Budget Request

For FY 1993, the budget request for Research Management and Support is $28,405,000, a net increase of $1,327,000 above the FY 1992 estimate. This increase represents funds required to support administrative cost increases, to fund centrally furnished services, and to contribute to various "taps" on the NIGMS budget. Funding for Research Management and Support during the last 5 years has been as follows:

	Amount	FTE
FY 1988	$17,837,000	141
FY 1989	20,416,000	145
FY 1990	22,395,000	152
FY 1991	22,717,000	165
FY 1992	27,078,000	170

During FY 1993, continued attention will be focused on enhancing management and administrative strategies to more effectively and efficiently fulfill the Institute's mission. For example, efforts will continue to automate additional grants management processes and to increase the scrutiny and documentation associated with analysis of grant budgets. Further development of databases to use in monitoring and evaluating grantees' progress will also be supported.

ICD: National Institute of General Medical Sciences

Detail of Permanent Positions

	1991 Actual	1992 Appropriation	1993 Estimate
ES-6	1	1	1
ES-4	3	3	3
ES-2	1	1	1
ES-1	1	1	2
Subtotal	6	6	7
GS/GM-15	16	17	17
GS/GM-14	17	18	18
GS/GM-13	18	18	18
GS-12	15	16	16
GS-11	1	2	2
GS-10	1	1	1
GS-9	14	15	15
GS-8	7	7	7
GS-7	23	25	25
GS-6	23	23	23
GS-5	13	13	13
GS-4	6	6	6
GS-3	1	1	1
Subtotal	155	162	162
Grades established by Act of July 1, 1944, 42 U.S.C. 207):			
Assistant Surgeon General			
Director Grade	1	1	1
Senior Grade			
Full Grade			
Senior Assistant Grade	2	1	1
Subtotal	3	2	2
Ungraded			
Total permanent positions	164	170	171

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

New Positions Requested

	1993		
	Grade	Number	Annual Salary
NIGMS Research Management and Support			
Health Science Administrator........	ES-1	1	$93,300

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

AMOUNTS BUDGETED FOR INCREASES IN
FULL-TIME EQUIVALENTS

ACTIVITY/POSITIONS	GRADE	NO. OF POS.	O.C. 11 ANNUAL SALARY	O.C. 12 BENEFITS @ 11.4%	O.C. 21 TRAVEL	O.C. 23 RENT, UTIL. & COMM.	O.C. 25 OTHER SERVICE	O.C. 31 EQUIPT.	OTHER OBJECTS	SUB.TOT. NEW COSTS	SUPPORT STAFF SHARE	NO. OF FTE	TOTAL NEW COSTS
NIGMS Program Support													
Health Science Administrator	ES-1	1	$93,330	$10,670	$3,000		$2,000			$109,000		1	$109,000

The increase of 1 FTE in FY 1993 is associated with employing the Program Director for the Biophysics and Physiological Sciences Branch.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Advisory and Assistance Services

For FY 1993, the Advisory and Assistance Services budget will be $903,000, an increase of $65,000 above FY 1992. These funds will continue to support a variety of services that are essential to the effective development and monitoring of existing programs. Services and studies included in the above categories are: support for a working group to provide scientific oversight of the Cell Bank; support for advice, assessments and evaluation of the Minority Access to Research Careers Program and the Minority Biomedical Research Support Program; assistance with various evaluation projects; and support for the National Advisory General Medical Sciences Council.

With the exception of the mandated Council activity, which must be performed by outside experts pursuant to law, the remaining activities noted above require the special scientific expertise and sensitive outside perspectives that representatives of the scientific community can bring to such activities. In addition, these are, by and large, time-limited activities for which it would be either be difficult or inappropriate to hire federal employees to perform.

The Institute requires that each request for professional services, as well as other contracts and purchase orders, be approved by the Director, NIGMS, or the Executive Officer, NIGMS, as the applicable delegations of authority specify. These approvals must be secured prior to the request being processed by the Administrative Office staff. The Director, NIGMS, and the Executive Officer, NIGMS, examine each request carefully for its appropriateness and adherence to regulations, including conflict-of-interest rules. Any contracts issued through the Delegated Procurement authorities by the Administrative Office, NIGMS, conform to all applicable regulations, including those dealing with a drug-free workplace, with the applicability of GAM 8-15 and Circular A-120, and with avoiding use of contracts to substitute for hiring government personnel. All persons involved in the Administrative and Executive Offices have received training in procuring such services, and regularly read NIH issuances and other updates or new regulations bearing on these activities.

TUESDAY, MARCH 24, 1992.

NATIONAL CENTER FOR RESEARCH RESOURCES

WITNESSES

DR. ROBERT A. WHITNEY, JR., DIRECTOR, NATIONAL CENTER FOR RESEARCH RESOURCES

JOHN D. MAHONEY, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH

DR. JUDITH L. VAITUKAITIS, DEPUTY DIRECTOR FOR EXTRAMURAL RESEARCH RESOURCES, NATIONAL CENTER FOR RESEARCH RESOURCES

DR. CAROLINE T. HOLLOWAY, DIRECTOR, OFFICE OF SCIENCE POLICY, NATIONAL CENTER FOR RESEARCH RESOURCES

RICHARD L. SHAFER, EXECUTIVE OFFICER, NATIONAL CENTER FOR RESEARCH RESOURCES

ANNE E. SUMMERS, BUDGET OFFICER, NATIONAL CENTER FOR RESEARCH RESOURCES

WILLIAM BELDON, BUDGET OFFICE, DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTRODUCTION OF WITNESSES

Mr. NATCHER. At this time we take up the budget request for the fiscal year 1993 for the National Center for Research Resources.

We have before the Committee Dr. Robert A. Whitney.

Dr. Whitney, it is a pleasure to have you before our Committee at this time.

Before you give us your statement, tell us who you have with you at the table.

Dr. WHITNEY. On my far right, Mr. William Beldon, representing Mr. Dennis Williams, from HHS, and Mr. Jack Mahoney, representing Dr. Healy, from NIH.

On my immediate right, is Dr. Judith Vaitukaitis, Deputy Director for Extramural Research Resources; Dr. Caroline Holloway, Director, Office of Science Policy; Richard Shafer, Executive Officer, and Anne Summers, Budget Officer.

Mr. NATCHER. Thank you very much.

Now Dr. Whitney, we will be pleased to hear from you.

OPENING STATEMENT

Dr. WHITNEY. Thank you, sir.

The National Center for Research Resources is a unique NIH component. It reaches thousands of investigators who are supported by NIH and the other PHS research agencies—scientists who work in all areas of biomedical and behavioral research throughout the Nation.

NCRR's mission is two-pronged. First, the Center supports primary research to develop new resources to ensure research advances and it also provides shared research resources to facilitate scientists' work.

These resources, together with NCRR activities to enhance research environments and capabilities at institutions across the Nation, are fundamental to NIH and PHS research and link us tightly to the research efforts of the other NIH Centers and categorical Institutes.

NCRR-supported research to develop resources ranges from animal and non-animal models to cutting-edge biotechnologies. NCRR must anticipate future directions and have in place the appropriate research resources to meet scientists' constantly evolving needs.

The Center's support for shared resources is primarily through resource centers, where research is conducted by more than 7,000 researchers, supported annually by well over $1,000,000,000 in NIH Research Institute's funds. These cost-effective resources include General Clinical Research Centers, Regional Primate Research Centers, and Biomedical Research Technology Centers.

In addition to the centers, NCRR also provides other research resources, such as animal models and other models to study human disease, and instrumentation crucial to biomedical research.

NCRR activities also enhance the Nation's biomedical research capability, helping to maintain our research competitiveness in the world. The Center carriers out programs that involve pre-college students and their teachers in research to develop the investigators of tomorrow; programs to develop and enhance the capacities of emerging institutions to participate in the research enterprise; and programs to improve the condition of research animal facilities.

The NCRR is a partner with each of the NIH Research Institutes and Centers in assuring the success of American biomedical research. They rely on sharing NCRR research resources and centers to support and facilitate the research of their grantees and contractors, thus substantially reducing the cost of biomedical research.

Last year the Committee took particular interest in NIH support for cancer research and research in Alzheimer's disease, as well as in AIDS research. These also continue to be high priorities for NCRR in 1993.

NCRR ranks third in support of the NIH AIDS research program, providing important resources for research involving patients infected with human immunodeficiency virus, or HIV, and research using animal models to study AIDS.

Especially important are studies in Macaque monkeys infected with the simian immunodeficiency virus, or SIV, which is remarkably similar to HIV. The SIV model was developed at NCRR-supported Regional Primate Research Centers and is widely used by investigators engaged in AIDS drug and vaccine development studies.

I am pleased to announce today that at our Washington Regional Primate Research Center an Asian Macaque monkey, the pigtail Macaque, has been infected for the first time with both types of human immunodeficiency virus, HIV-1 and HIV-2.

This offers promising new avenues of AIDS research along with the chimpanzee breeding and research program.

A look at other research areas illustrates the broad impact of NCRR's research resources on NIH research. Over $40,000,000 of NCRR resources support neuroscience research on Alzheimer's disease, Parkinson's disease, and other neurological disorders.

Cancer, heart disease, diabetes, nutrition, and digestive diseases are other important focal points for scientists, who rely on NCRR's research resources.

In these, and all biomedical research areas, modeling is a fundamental tool, important for developing information and explanations that lead to the logical next step. Modeling is especially important in developmental biology, research on disease states and their treatments, and research on biological and biochemical processes.

NCRR's mission demands that we foster collaborative and multidisciplinary research modeling. For example, existing animal models are being made more useful by researchers who are developing technologies such as identical twinning through splitting of animal embryos and DNA micro-injection of embryonic stem cells. This also facilitates the search for new model systems among lower animals.

Studies of rare diseases present unique opportunities for correlating the molecular basis of disease with clinical observations. Technical advances can lead to earlier diagnosis of genetic disease, and consequently to improved treatments or to new treatments such as gene therapies.

The General Clinical Research Centers continue to be the optimal environment for studies of rare diseases, which affect about 12,000,000 Americans. Twenty to 25 percent of the more than 4,500 research projects conducted at the GCRCs involve the study of rare diseases, and these studies are enhanced by rare disease "referrals" and shared data among investigators using this network of centers.

As a result of this collaboration, more advances in conditions such as Fabry's disease, sickle cell anemia, and cystic fibrosis can be expected.

NCRR leads the Nation in the development and provision of high technology research resources through its Biomedical Research Technology Program. In 1993, the BRT program will continue to develop technologies and provide resource centers where biomedical investigators share state-of-the-art resources and newer technologies are enhanced to create ever more powerful instrumentation.

The tremendous growth in knowledge about the molecular basis for disease has led to a more rational basis for designing new therapeutic agents, and much of this knowledge was derived from new physical or chemical techniques developed through the BRT program.

For example, a very important recent advance was the determination of the structure of the intracellular messenger, protein P-21, in both its turned "on" and turned "off" configurations—at atomic resolution. Cells reproduce excessively—a characteristic of cancer—when this protein stays "on" too long.

Knowledge of the protein's structure has created a burst of drug design activities based on an exact knowledge of the molecular shape required to turn it "off." This advance depended on the newly available technologies in synchrotron X-radiation, high-speed X-ray detectors, and high-performance computing and algorithms.

NCRR also continues to emphasize its programs that address the critical need to bring minority research institutions into the mainstream of America's biomedical research efforts. Our Research Centers in Minority Institutions Program represents the country's single most important effort to bring doctoral-degree-granting minority institutions into full partnership in the Nation's biomedical research activities. We have provided examples of exciting, new research activities at these schools in our written justification. We are proud of our role in the expansion of their research programs, as these institutions continue to increase their contributions to the discovery of new knowledge and the advance of medicine.

This year, as in 1992, funds are being requested for the Research Facilities Improvement Program. This program, which would provide funds for the construction and major renovation of research facilities at Historically Black Colleges and Universities and similar institutions, is a critical component in NIH's commitment to bringing the research capabilities of minority institutions to a level which would afford them full participation in the biomedical research effort.

The effect of this program would be to broaden the base of American institutions that conduct research and would ultimately enhance all NIH programs.

NCRR is also making major contributions in the critical area of science education. We know we must do everything in our power to attract young people to careers in science and mathematics.

One of the most productive ways to do this is to involve minority high school students and science teachers of minority students in hands-on research at nearby colleges and universities through the Minority High School Student Research Apprentice Program.

Fiscal year 1993 will be the 13th year of the program; we anticipate that approximately 3,000 high school students and 575 science teachers will participate in this enrichment program in 1993.

In 1991, NCRR spearheaded the implementation of the Science Education Partnership Award, a program that made grants to 12 institutions to stimulate the interest of kindergarten through 12th grade students in science, especially biology, and to increase the level of science literacy in all of our Nation's people.

For fiscal year 1992, the NCRR, with the advice and assistance of our National Advisory Research Resources Council, redesigned the Biomedical Research Support Grant Program. The new design calls for competing awards of $50,000 each in direct costs—BRS grants do not include payments for overhead costs.

The competitive review will be conducted by an NIH administrative group, with second level review by the NCRR council. We have focused the objectives of this program on a single major category of needs rather than the broader portfolio of uses that historically characterized this program. This year BRSG fund will only be awarded to support biomedical research projects in ways that are not adequately or efficiently provided by other funding mechanisms such as the traditional investigator-initiated research project award.

We expect and encourage use of these funds for pilot research that may provide the basis for research project grant applications, for the initial research support of new investigators, and for unexpected requirements and opportunities within research projects supported by other NIH funding mechanisms, such as funding to enable promising research programs to continue during temporary lapses of project grant support.

In fiscal year 1992, NCRR will fund two new Biomedical Research Technology Centers in high performance computing and communications. The rapid increase in computational power of today's computers is creating exciting new opportunities in several biomedical research areas, including molecular dynamics, protein structural analysis, and quantitative image analysis.

NCRR funding for these new centers will support the development of new methods and algorithms required to use high performance computers effectively. Computer-based modeling has proven effective in predicting protein configuration, and it may soon be possible for computer-aided predictions to extend the limits set by existing experimental methods.

An especially interesting application may be the analysis of brain maps and the exploration of new techniques, such as neural networks. These new methods could have a major impact on areas such as rational drug design and unravel such fundamental processes as binding of a protein to DNA and protein folding.

In fiscal year 1992, funds were provided to support additional synchrotron resources. One new resource is located at the University of Chicago, where NCRR proposes to construct two beam lines for biomedical research use at Argonne National Laboratories advanced photon source, a Department of Energy facility. The NIH users will focus on structural studies of viruses and on new time-resolved X-ray diffraction studies of proteins that need the very high energy of the Advanced Photon Source.

NCRR has provided long-time support for the three existing synchrotron resource centers for structural biology studies by biomedical researchers. Nevertheless, many scientists have had to travel to synchrotron laboratories in Europe and Japan because sufficient time was not available for biomedical research use at U.S. centers. Our investment in 1992 and its carryover into 1993, will help to provide U.S. scientists with more domestic access to these new synchrotron radiation facilities.

Mr. Chairman, the fiscal year 1993 request for the National Center for Research Resources is $330,231,000.

I will be pleased to answer your questions.

[The statement of Dr. Whitney follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement of the Director

National Center for Research Resources

Mr. Chairman and members of the Committee: The National Center for Research Resources (NCRR) is a unique agency of the National Institutes of Health (NIH) reaching thousands of investigators supported by NIH and the other Public Health Service (PHS) research agencies working in all areas of biomedical and behavioral research throughout the Nation.

NCRR's mission includes both primary research to develop resources to assure research advances and shared research resources to facilitate biomedical research of scientists receiving support from the NIH and other PHS agencies. The development of new research technology and provision of shared biomedical resources, together with NCRR activities to enhance research environments and capabilities of institutions across the Nation, is fundamental to NIH research. NCRR assures that the appropriate infrastructure is accessible to scientists supported by the NIH and PHS institutes, and this links us inextricably to the research efforts of the other NIH centers and categorical institutes.

NCRR-supported research to develop resources ranges from animal and non-animal models to cutting edge biotechnologies. NCRR must anticipate future directions and have in place the appropriate research resources to meet scientists' constantly evolving needs.

NCRR also supports shared resources, primarily resource centers, where over 7,000 researchers, supported by well over $1 billion of NIH research institute funds, conduct their research. These proven cost effective resources include General Clinical Research Centers (GCRC), Regional Primate Research Centers (RPRC), and Biomedical Research Technology Centers. NCRR also provides other research resources, such as animal and other models to study human disease, and technologies and instrumentation necessary to facilitate biomedical research.

NCRR activities assure the enhancement of the Nation's biomedical research capability, to maintain our research competitiveness in the world. NCRR carries out programs to involve pre-college students and their teachers in research to develop the investigators of tomorrow, to develop and enhance the capacities of emerging institutions to participate in the research enterprise, and to improve the condition of research animal facilities.

The NCRR is a partner with each of the NIH research institutes and centers in assuring the successful accomplishment of biomedical research throughout the Nation. They rely on sharing NCRR research resources and centers to support and facilitate the research of their grantees and contractors, thereby substantially reducing the cost of biomedical research.

Last year the Committee took particular interest in NIH support for cancer research and research in Alzheimer's disease, as well as in AIDS research. These continue to be high priorities for NCRR in 1993. NCRR ranks third in support of the NIH AIDS research program, providing important resources for research involving patients with human immunodeficiency virus (HIV) infection. These funds support the AIDS research effort by studying non-human primates and the progression of simian immunodeficiency virus (SIV) in macaque monkeys, as well as HIV in chimpanzees. The SIV model was developed at NCRR-supported regional primate research centers and is widely used by investigators engaged in AIDS research. The NCRR-supported National Chimpanzee Breeding and Research Program provides the source of animals to scientists for vaccine development and testing. Support in other research areas illustrates the broad impact of NCRR's research resources on the conduct of research by NIH. Over $40 million of NCRR resources also support neuroscience research including Alzheimer's disease, Parkinson's disease, and other basic neurosciences research. Cancer and heart research and research on diabetes, nutrition, and digestive diseases are other important foci for scientists who rely on NCRR's research resources.

NCRR's mission and its trans-NIH mandate require that it serve as the focus for collaborative and multidisclipinary research modeling, drawing on the knowledge of the NIH community and the leadership and expertise of the NCRR staff. Biological modeling is important in developing all the theoretical aspects of biology, particularly in such areas as developmental biology, research on disease states and their treatment, research on biological and biochemical processes, molecular processes and the bio-mechanical properties of tissues and organs. Similarly, developing and using evolving technologies such as identical twinning through splitting of animal embryos, and DNA micro-injection of embryonic stem cells, allow investigators to characterize existing animal models more rapidly, and facilitate the search for new model systems among lower animals.

Studies of rare diseases present unique opportunities for correlating the molecular basis of disease with clinical observations. Technical advances can lead to earlier diagnosis of genetic disease, and consequently to improved treatments or to new treatments such as gene therapies. The GCRCs continue to be the optimal environment for studies of rare diseases. Twenty to 25 percent of the more than 4,500 research projects conducted at the GCRCs involve the study of rare diseases, and these studies are enhanced by rare disease "referrals" and shared data among investigators using this network of centers. As a result of this collaboration, more advances in diseases such as Fabry's, Sickle Cell Anemia, and cystic fibrosis can be expected.

NCRR leads the Nation in the development and provision of high technology research resources through its Biomedical Research Technology (BRT) Program. In 1993, the BRT Program will continue to develop technologies and provide resource centers where biomedical investigators share state-of-the-art resources, and newer technologies are enhanced to create ever more powerful instrumentation. The tremendous growth in knowledge about the molecular basis for disease, much of it derived from new physical or chemical techniques developed through the BRT Program, has led to a rational basis for designing new therapeutic agents. A most recent advance depended on the newly available technologies in synchrotron X-radiation, high speed X-ray detectors, and high performance computing and algorithms to determine the structure of the intracellular messenger protein p21 in both its "on" and "off" configurations--at atomic resolution. Cells reproduce excessively -- a characteristic of cancer -- when this protein stays "on" too long. Knowledge of the protein's structure has created a burst of drug design activities based on an exact knowledge of the molecular shape required to turn it "off."

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This year, as in 1992, funds are being requested for the Research Facilities Improvement Program. This Program, which would provide funds for the construction and major renovation of research facilities at Historically Black Colleges and Universities (HBCUs) and similar institutions, is a critical component in NIH's commitment to bring the research capabilities of minority institutions to a level which would afford those institutions full participation in the biomedical research effort. The effect of this Program would be to broaden the base of institutions that conduct research and would ultimately enhance all NIH programs. NCRR is also making major contributions in the critical area of science education. We know we must do everything in our power to attract young people to careers in science and mathematics. One of the most productive ways to do this is to involve minority high school students and science teachers of minority students in hands-on research at nearby colleges and universities through the Minority High School Student Research Apprentice Program. FY 1993 will be the 13th year of the program; we anticipate that approximately 3,200 high school students and 500 science teachers will participate in this enrichment program.

In 1991 NCRR spearheaded the implementation of the Science Education Partnership Award, a program which made grants to twelve institutions to stimulate the interest of kindergarten through twelfth grade students in science, especially biology, and to increase the level of science literacy in all of our Nation's people.

For FY 1992 the NCRR, with the advice and assistance of our National Advisory Research Resources Council, redesigned the Biomedical Research Support Grant (BRSG) Program. The new design calls for competing awards of $50,000 each in direct costs (BRSG grants continue to not include payments for overhead costs). The competitive review will be conducted by an NIH administrative group, with second level review by the Council. We have focused the objectives of this Program on a single major category of needs rather than the broader portfolio of potential uses that historically characterized this program. This year BRSG funds will only be awarded to support biomedical research projects in ways that are not adequately or efficiently provided by other funding mechanisms such as the traditional investigator-initiated research project award. We expect and encourage use of these funds for pilot research that may provide the basis for research project grant applications, for the initial research support of new investigators, and for unexpected requirements and opportunities within research projects supported by other NIH funding mechanisms, such as funding to enable promising research programs to continue during temporary lapses of project grant support.

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In FY 1992 funds were provided to support additional synchrotron resources. One new resource is located at the University of Chicago where NCRR proposes to construct two beamlines for biomedical research use at Argonne National Laboratories Advanced Photon Source (APS), a Department of Energy facility. The NIH users will focus on structural studies of viruses and on new time-resolved X-ray diffraction studies of proteins that need the very high energy of the APS.

NCRR has provided long time support for the three existing synchrotron resource centers for structural biology studies by biomedical researchers. Nevertheless, many scientists have had to travel to synchrotron laboratories in Europe and Japan because sufficient time was not available for biomedical research use at U.S. centers. Our investment in 1992 and its carry-over into 1993 will help to provide U.S. scientists with domestic access to these new synchrotron radiation facilities.

Mr. Chairman, the FY 1993 request for the National Center for Research Resources is $330,231,000. I will be pleased to answer your questions.

BIOGRAPHICAL SKETCH
Robert A. Whitney, Jr., D.V.M.
Director, National Center for Research Resources

Birthdate: July 27, 1935 - Oklahoma City, Oklahoma

Education: D.V.M., Oklahoma State University College of Veterinary Medicine, 1959; M.S. (Pharmacology), The Ohio State University, Graduate School, 1965; Resident in Laboratory Animal Medicine, The Ohio State University College of Medicine, 1965.

Professional History: 1990 to present, Director, National Center for Research Resources, NIH; 1988 to 1990, Acting Director, Division of Research Resources, NIH; 1987 to present, Director, Office of Animal Care and Use, NIH; 1985 to 1990, Director, Division of Research Services (DRS), NIH; 1984 to 1989, Chief Veterinary Officer, U.S. Public Health Service (USPHS); 1984 to present, Chairman, U.S. Government Interagency Research Animal Committee (IRAC); 1984-1985, Acting Director, Division of Research Services (DRS), NIH; 1972-1985, Chief, Veterinary Resources Program, DRS, NIH;

Uniformed Service: 1971 to present, U.S. Public Health Service, Assistant Surgeon General (Rear Admiral, 08); 1959-1971, United States Army (Lieutenant Colonel, 05).

Societies and Associations: American Association for Laboratory Animal Science; American Association of Laboratory Animal Practitioners; American College of Laboratory Animal Medicine; American Society of Primatologists; American Veterinary Medical Association; Commissioned Officers Association, USPHS; District of Columbia Veterinary Medical Association; National Capital Area Branch, American Association for Laboratory Animal Science; The Scientific Research Society of America; Association of Military Surgeons of the United States.

Honors and Awards: USPHS Distinguished Service Medal; USPHS Surgeon General's Exemplary Service Medal; USPHS Meritorious Service Medal; USPHS Commendation Medal; Department of Army Legion of Merit; Department of Army Meritorious Service Medal; Department of Army Commendation Medal; NIH Director's Award; Ohio State University College of Veterinary Medicine, Distinguished Alumnus Award; Oklahoma State University College of Veterinary Medicine, Distinguished Graduate Recognition Award; The Charles River Prize; Alpha Zeta; Blue Key; included in 1973 Edition, American Men and Women of Science; Diplomate, American College of Laboratory Animal Medicine.

Publications: Author of one book and over 40 scientific papers.

NIH STRATEGIC PLAN

Mr. NATCHER. Thank you, Dr. Whitney.

Now, Doctor, how does the mission of your center fit into the proposed NIH strategic plan?

Dr. WHITNEY. We feel that we can be important players in the strategic plan in a number of ways. First, the four critical technologies listed in the plan, molecular medicine, biotechnology, vaccine development and structural biology, all will require the shared resources of the NCRR.

The biotechnology centers, shared instrumentation, the clinical research centers, and the primate centers, all will be active players. As you know, the primate centers are particularly active in the vaccine development work against AIDS.

Certainly, NCRR will play a very key role in the research capacity building part of the strategic plan, developing research capability through development of infrastructure across the Nation and sharing resources.

In the intellectual capital area, as I mentioned earlier, the science education program, our high school training programs, and the programs in training clinical and other researchers will help develop that important aspect of the plan.

We feel we will be key players in all elements of the NIH proposed strategic plan.

SHARED RESOURCES

Mr. NATCHER. Do you have any estimate of how much NIH saves by providing shared resources through your programs rather than funding them individually?

Dr. WHITNEY. No, sir, I cannot answer that question definitively. Looking at the numbers of investigators that are using the shared resources and the fact that they are sharing, there has to be a great amount of savings versus a research project that would have to provide its own infrastructure. For example, an average of eight researchers share each instrument awarded in the shared instrumentation grant program.

BIOMEDICAL RESEARCH TECHNOLOGY

Mr. NATCHER. Last year you indicated that funding for the Biomedical Research Technology Program was your top priority, even above restoring cuts in other areas.

Do you still feel the same way, Dr. Whitney?

Dr. WHITNEY. No, sir. We did receive a very significant increase in our Biomedical Research Technology Program in 1992.

We feel our top priority for 1993 has to be meeting current services for our shared resource programs so that we can keep them linked to the research project grants that require their support.

If the research project grants grow at a faster rate than our shared resources, I think we all suffer.

BIOMEDICAL RESEARCH SUPPORT GRANTS

Mr. NATCHER. In its 1992 report, the Senate suggested you request additional funding for biomedical research support grants from the Director's contingency fund. Did you do that?

Dr. WHITNEY. We requested it but the fund was used for other things, including the Shannon Awards.

Mr. NATCHER. Describe, if you will, your new system for allocating biomedical research support grants now that the funding totals about $5,000,000.

Dr. WHITNEY. As I mentioned in my opening statement, we have started a new type of award because there were about 630 institutions eligible for the biomedical research support grants, while there is only about $5,200,000 in the 1992 and 1993 budget. We reconfigured the program and divided the eligible institutions into three equal tiers: those currently receiving the largest amount of money from NIH, a group in the middle, and then the smaller recipients of NIH grants.

We intend to have the institutions in those three tiers compete against their own tier members for $50,000 awards. These awards will only go to about 104 institutions but the $50,000 will be a meaningful amount of money.

The awards will have to be associated with biomedical research activity in some respect, such as pilot studies or bridge grants to support new investigators.

There will be a competitive mechanism for this, and we will ask for an indication on the part of the recipient institution of their commitment to provide matching funds.

Mr. NATCHER. Is total biomedical research support grant funding now so low, Doctor, that the program has lost its effectiveness?

Dr. WHITNEY. I certainly believe it has lost its effectiveness at the 630 institution level. However, we believe the $50,000 awards to 104 institutions can do a great deal of good.

SYNCHROTRON FACILITIES

Mr. NATCHER. Your biomedical research technology program emphasizes the importance of synchrotron facilities. How is your support of these facilities different, Doctor, from that of the Energy Department?

Dr. WHITNEY. The Energy Department provides the funds to build the basic facilities. We supply funds to provide the "ports" to be used by biomedical researchers. Beam lines emanating from the synchrotron are available through our support which would be complementary to the DOE program.

The DOE provides the big-ticket items and we provide the access funds for biomedical researchers to use this essential technology. We have both the provision for the construction of the beam line and then the follow-up costs to operate it over the years.

Mr. NATCHER. Doctor, why are these centers so important to biomedical research?

Dr. WHITNEY. The use of X-ray diffraction and high-intensity light sources is essential to look at the structure of proteins, including viruses and now even larger proteins. It allows us to actually see what the protein structure looks like.

Once the structure of a virus, for example, is established, then other technologies allow us to develop ways to inactivate it. We can then design drugs based on the viral and protein structures we now know from the synchrotron radiation research.

Mr. NATCHER. Mr. Pursell, I will yield to you.

RESOURCES PROVIDED TO NIH ICDS

Mr. PURSELL. Thank you.

Your program provides resource materials and scientific research resources?

Dr. WHITNEY. Yes. We provide a home, so to speak, to provide research resources to all of the NIH Institutes.

Mr. PURSELL. But you are really supporting Institutes by providing resources projects? Could you illustrate?

Dr. WHITNEY. As an example, you have the clinical research center at Ohio State University. That is a small research hospital within the hospital structure of the university, where beds dedicated to research, research nurses, nutritionists, mathematicians, laboratories for diagnostics, and computer access are all provided to researchers who have grants from other categorical Institutes in the NIH to perform research at the center.

If an investigator is going to do a clinical AIDS study funded by NIAID the chances are good that they will be using one of our clinical research centers.

Mr. PURSELL. For both investigators, lab and the personnel?

Dr. WHITNEY. It works in different ways, ranging from direct collaboration to providing the services and resources that are needed.

Mr. PURSELL. Do you supply personnel?

Dr. WHITNEY. We supply personnel, who do the nutrition work, and the research nurses. Our biggest single cost is nursing, providing research nurses who are capable of handling the types of patient that would be on our GCRC.

Mr. PURSELL. You are a pool of resources?

Dr. WHITNEY. Yes, sir, a critical mass. Investigators who are applying to categorical Institutes, for example, for support for clinical research, do better if they are associated with an institution that has a general clinical research center. That grant is going to be more cost effective.

ANIMAL RESOURCES

Mr. PURSELL. If it includes clinical labs where they would need animals, chimpanzees or mice, do you supply those? Are you the provider?

Dr. WHITNEY. We don't provide animals in the traditional manner. The cost of those animals is a direct cost of research grants.

Mr. PURSELL. You have no animal laboratories?

Dr. WHITNEY. Yes, we have animal laboratories, including the seven regional Primate Research Centers. They are particularly active in supporting hundreds of NIH investigators who use our animals on our premises. In other words, again, it is a critical mass of resources.

Mr. Pursell. If they have a project and they need "X" number of chimpanzees, you would provide that?

Dr. Whitney. That is correct, and it would more likely be done in our facilities.

Mr. Pursell. Which Institute under the NIH umbrella has the most animal laboratories? Would that be you?

Dr. Whitney. Yes, I suppose it would. We also support colonies of animals that are provided for research.

Let me give you an example: We provide the small round worms that are used for genetic research in the human genome project. This very small round worm, call *C. elegans,* is available from the University of Missouri. With our support, they are made available to researchers around the country.

We don't actually provide most mammalian models, with the exception of a few special rodent colonies. We do provide research infrastructure to do research on animal models.

Mr. Pursell. What about the debate that developed some years ago with respect to animal rights groups and the use of chimpanzees? Were you impacted with that, and aren't you doing some studies to reduce the number of chimpanzees in clinical trials?

Dr. Whitney. We are maintaining a critical mass of chimpanzees in this country, a breeding group that will be self-perpetuating.

Mr. Pursell. How many would that be?

Dr. Whitney. The total colony is currently about 480 animals in five different colonies around the country. We have had about 250 baby chimpanzees since we started the program in 1986.

Half of those are kept for breeding and the others are available for research. They may be returned to the colonies later if they are not carrying hepatitis C, HIV, or other infectious agents.

We know we must have the colonies to be sure we never have to return to the wild for chimpanzees.

We are also looking at ways to minimize the use of chimpanzees. Using the SIV model in Macaque monkeys, we have been able to do a lot of preliminary work on vaccines and on the general effect of immunodeficiency virus before we move to HIV in chimpanzees.

Up until the last few weeks, the chimpanzee has been the only animal susceptible to the HIV, Human immunodeficiency virus, Type I. Now we have a Macaque monkey that is also susceptible to the HIV virus.

NCRR RESEARCH

Mr. Pursell. So you are essentially the basic supplier in support of a supplement of the Institutes to do research. You, yourself, do not do any research per se?

Dr. Whitney. Yes, we do. For example, within the biotechnology centers in particular, there has to be the experimental development of new instrumentation, including design and bringing the instrument up to commercial application.

Some of the people doing research in those centers and in our Regional Primate Research Centers are funded by us and do the research with our funds. It is a combination. We provide shared resources, and directly support research that is being done as well.

Mr. PURSELL. What is your total research budget for clinical trials and basic research?

Dr. WHITNEY. It is at this point so interwoven with the trans-NIH research efforts that it would be difficult to break that out.

Mr. PURSELL. It is $330,000,000?

Dr. WHITNEY. Right. That is our total NCRR budget.

Mr. PURSELL. Are you talking about 10 percent?

Dr. WHITNEY. I would say within the resource centers we are talking about 20 to 30 percent.

RESOURCE CENTERS

Mr. PURSELL. You have 201 centers?

Dr. WHITNEY. Our centers are about 75 percent of our total program.

Mr. PURSELL. Are all the centers located at universities?

Dr. WHITNEY. Almost all of them are.

Mr. PURSELL. Is there any practical value or any sense to having some of those centers in the inner cities or in outreach programs where they would be more directly related today to what I will call, the real world?

Dr. WHITNEY. Many institutional settings are in the larger cities. Our general clinical research centers are in areas where they do have outreach to the local communities. Our research centers in minority institutions have a large outreach capacity for minorities.

Mr. PURSELL. When you say minority institutions, you mean minority universities?

Dr. WHITNEY. The 17 institutions that make up the Research Centers in Minority Institutions program all have 50 percent or more minority student body and all grant doctoral degrees in health sciences. They are located across the continental U.S. and in Puerto Rico and Hawaii.

Mr. PURSELL. Will you provide a listing of where they might be and some examples of what their mission is and who they relate with?

Dr. WHITNEY. Yes.

Mr. PURSELL. Give us two or three good examples of what their function and role is.

[The information follows:]

NATIONAL CENTER FOR RESEARCH RESOURCES

The function and role of the 17 Research Centers in Minority Institutions is the development of appropriate infrastructure to conduct biomedical research, particularly in areas that disproportionately affect minority populations. The 17 Centers, their location, and their research foci are as follows:

1. Atlanta University Graduate School, Atlanta, Georgia - molecular biology, biochemistry, molecular genetics, virology, immunology, developmental biochemistry

2. City College of New York, New York, New York - cellular and molecular basis of development, biomolecular structure and function, gene expression and regulation, cell and organism function

3. Hunter College, New York, New York - gene structure and function, developmental neurobiology, immunology

4. Drew Postgraduate Medical School, Los Angeles, California - hypertension, behavioral and perinatal disease

5. Florida A&M University School of Pharmacy, Tallahasee, Florida - human drug studies, drug design research

6. Howard University Medical School, Washington, D.C. - immunogenetics, veterinary pathology, biostatistics

7. Morehouse Medical School, Atlanta Georgia - cancer, cardiovascular disease, immunology and neuroscience

8. Texas Southern University, Houston, Texas - diabetic nephropathy, hypertension, sickle cell anemia

9. University of Puerto Rico, San Juan, Puerto Rico - protein analysis, AIDS

10. Tennessee State University, Nashville, Tennessee - biomedicine, behavior

11. University of Hawaii, Honolulu, Hawaii - cell biology, molecular biology, biotechnology, neurobehavioral biology, mental health research

12. Universidad Central del Caribe, Bayamon, Puerto Rico - gastroenterology, neurosciences

13. Xavier University of New Orleans, New Orleans, Louisiana - diabetes, hypertension, medical sociology

14. Meharry Medical School, Nashville, Tennessee - AIDS, immunology, virology, gene therapy

15. Ponce Medical School, Ponce, Puerto Rico - environmental toxicology, clinical immunology, AIDS

16. University of Puerto Rico, Rio Piedras, Puerto Rico - cell and molecular biology, photochemistry, photobiology

17. Tuskegee Institute, Tuskegee, Alabama - in vitro modeling, computer modeling, animal modeling

Mr. Pursell. Thank you, Mr. Chairman.

Mr. Natcher. Mr. Stokes, I yield.

MINORITY CONSTRUCTION

Mr. Stokes. Dr. Whitney, the 1993 request includes $12,000,000 in construction funds for Historically Black Colleges and Universities. What is the present status of NCRR authority to make grants at black colleges and institutions?

Dr. Whitney. We have no construction authority.

Mr. Stokes. You need an authorization?

Dr. Whitney. Yes, sir.

Mr. Stokes. If they are approved, how much will be added to the RCMI budget?

Dr. Whitney. Funds will not be added directly to the RCMI budget, but these institutions will be highly competitive for this program. The competition will be based on existing research capabilities and plans to engage in biomedical research within the institutions that will be funded. The RCMI institutions will be well positioned to compete for this money.

RESEARCH CENTERS IN MINORITY INSTITUTIONS PROGRAM

Mr. Stokes. In terms of the RCMI program, how many institutions have now received awards?

Dr. Whitney. Seventeen.

Mr. Stokes. What funding is in the budget for this program?

Dr. Whitney. For the RCMI program?

Mr. Stokes. Yes.

Dr. Whitney. $23,574,000 is requested in 1993.

Mr. Stokes. Is this the same amount for 1992?

Dr. Whitney. Yes.

Mr. Stokes. So it is level funding?

Dr. Whitney. Yes, sir.

Mr. Stokes. For the record, would you provide for me the 17 schools which are grantees, how many are predominantly black, Hispanic, Asian, and Pacific islanders, et cetera, identify those schools for the record?

[The information follows:]

The 17 Research Centers in Minority Institutions and their predominant ethnic minority make-up are as follows:

1. Atlanta University Graduate School—Black.
2. City College of New York—Black, Hispanic.
3. Hunter College—Black, Hispanic.
4. Drew Postgraduate Medical School—Black.
5. Florida A&M University School of Pharmacy—Black.
6. Howard University Medical School—Black.
7. Morehouse Medical School—Black.
8. Texas Southern University—Black.
9. University of Puerto Rico, San Juan—Hispanic.
10. Tennessee State University—Black.
11. University of Hawaii—Asian and Pacific Islander.
12. Universidad Central de Caribe—Hispanic.
13. Xavier University of New Orleans—Black.
14. Meharry Medical School—Black.
15. Ponce Medical School, Puerto Rico—Hispanic.
16. University of Puerto Rico, Rio Piedras—Hispanic.
17. Tuskegee Institute—Black.

Mr. STOKES. As a result of the RCMI programs, some important collaborative programs have emerged. Will you share some of this with the Committee?

Dr. WHITNEY. We have been very pleased with the leveraging of the RCMI dollars with other Institutes. We have been very happy that the National Institute of Allergy and Infectious Diseases has provided co-funding to us in the AIDS research area. They are providing funds so that three of our RCMI institutions can develop the infrastructure to participate in AIDS clinical trials. That is an important collaboration.

Dr. McNairy has been working on developing collaborations with a number of other institutes. We have held symposia with the National Center for Human Genome Research, the National Institute of Environmental Health Sciences, the National Institute for Dental Research, and the National Institute for Diabetes, Digestive and Kidney Diseases, to develop the capacity of RCMI institutions to better compete for their funds. Co-funding has been developed between RCMI and the human genome program; and, more recently there has been an agreement with the National Institute of Dental Research to co-fund development of three minority dental research centers at institutions that are part of the RCMI program.

Mr. STOKES. In terms of your funding for the RCMI program, what was the amount you requested from the Department for this program?

Dr. WHITNEY. Our request to NIH for RCMI was $35,585,000.

Mr. STOKES. So, the amount you are asking for under this budget, $23,600,000 is the amount OMB provided. Is that right?

Dr. WHITNEY. I could not tell you where it was cut, but it is a reduction from our original request.

Mr. STOKES. Do you plan to fund any new RCMI applications in fiscal year 1993?

Dr. WHITNEY. The budget will not allow us to fund any new RCMI applications in 1993.

CO-FUNDING OF RCMI PROJECTS

Mr. STOKES. Concerning the impact and need for co-funding of RCMI projects, a few years ago, NIAID developed the request for applications to broaden the AIDS clinical trials group to include the under-representation of minorities in AIDS clinical trials. Has this initiative expanded clinical investigations and increased the participation of minority institutions?

Dr. WHITNEY. Yes, it certainly has. We have had a very significant infusion of dollars from NIAID in 1992, a total of $3,700,000, to three RCMI institutions—Howard, the University of Hawaii, and the University of Puerto Rico—for AIDS clinical trial support.

Mr. STOKES. Are there any plans for continuing this initiative beyond the three years of approved funding?

Dr. WHITNEY. I hope so.

Mr. STOKES. NIH has encouraged ADAMHA and other Institutes to better utilize the RCMI program. What has been the record to date, apart from the NIAID, on this?

Dr. WHITNEY. We have planning in process with NIDDK. We have not been involved with the ADAMHA Institutes.

We have been actively soliciting support and co-funding from the National Institute of Environmental Health Sciences. We have one grant from the National Center for Human Genome Research, and we are hoping to do more in that area. Things are starting to move in co-funding and in the RCMI institutions' ability to compete independently for funds from other Institutes.

Mr. STOKES. You mentioned co-funding. I wanted to ask you, what are the plans for expanding RCMI's co-funding activities, including institutions which specialize in diseases impacting minority populations, such as infant mortality, diabetes, hypertension, et cetera?

Dr. WHITNEY. Within NCRR, we are working on collaborative research with the general clinical centers. In California, at the Charles R. Drew Postgraduate Medical School, we are studying hypertension in minority populations. We are developing a collaboration between Meharry's and Vanderbilt's clinical research centers, the University of Hawaii's program and the University of San Francisco's clinical outreach centers. This is with RCMI participation so that programs may reach further into the minority community.

Mr. STOKES. To what extent is the Center addressing the needs of the RCMI and institutions to conduct clinical research?

Dr. WHITNEY. What we have at this point is primarily the collaboration between the existing general research centers and the RCMI programs. Other than our traditional infrastructure support, we have not made a specific effort to increase the capabilities for clinical research within the RCMI funding.

REGIONAL PRIMATE RESEARCH CENTERS

Mr. STOKES. I see the request includes $3,000,000 to continue to address repair and renovation needs of the regional primate centers. How does this level of funding compare to the amount provided last year?

Dr. WHITNEY. $3,000,000 was provided last year. That amount has been a part of the core budget for several years for the primate centers.

Mr. STOKES. Do you have data on what total amount of funding is needed to address these needs?

Dr. WHITNEY. I can tell you what the estimate is, based on requirements to meet USDA regulations approved a year ago: $35,000,000 to $40,000,000 was the figure the primate centers cited as the cost to implement the USDA regulations for primate holding.

MINORITY HIGH SCHOOL PROGRAM

Mr. STOKES. I notice the minority high school program, which encourages minority students to pursue careers in research-related health care. Can you tell us how this program is conducted?

Dr. WHITNEY. The minority high school student research apprentice program has been going now for about 13 years. The award is a one-year grant to any institution that is eligible for our biomedical research support grant or the minority biomedical research support grant. We support an average of 7.5 students and 1.5 teachers per institution in those institutions that have been awarded the dollars, about 400 institutions. These institutions provide opportunities for hands-on research experience to both students and teachers.

Salary is paid for the teacher and the student, and funds are provided for expenses to support the position. This year we will support about 3,000 students and nearly 600 teachers in this program. We think this is a wonderful program.

Three of the Westinghouse Science Talent Search finalists this year were participants in our program for minority high school students. We are proud of that.

Mr. STOKES. How are these students selected?

Dr. WHITNEY. They are selected by the institutions involved. We review the institution's plan on how it will develop and use the program, but the actual selection is done at the institutional level.

Mr. STOKES. To what extent do science teachers participate in this program?

Dr. WHITNEY. We started last year with high school science teachers, and we supported several hundred. In 1992, we will support 575 science teachers. This year they will be not only science teachers primarily of minorities in high school, but also junior high and grade school science teachers.

MINORITY EMPLOYMENT

Mr. STOKES. In terms of your Institute, Doctor, what percentage of the employees in your Institute are minorities?

Dr. WHITNEY. About 40 percent.

Mr. STOKES. Are they spread across the board in terms of your grade levels?

Dr. WHITNEY. Yes, they are, and about 9 percent of our total work force are minorities in the research categories. We have a good distribution of minorities and women.

Mr. STOKES. Feel free to expand upon that question in the record.

Dr. WHITNEY. I will.

[The information follows:]

The distribution of NCRR full time permanent employees by grade band and ethnic group is as follows:

Grade band	Asian/Pacific Islander	Black	Hispanic	Non-minority	Total
GS-1 to 4	1	14	2	14	31
GS-5 to 8	4	62	3	83	152
GS-9 to 12	5	34	0	86	125
GS/GM-13 to 15	2	15	1	60	78
Executive Service	0	0	0	2	2
Commissioned Corps	0	2	0	13	15
Fellows	5	1	0	9	15
Wage system	2	40	0	43	85
Total	19	168	6	310	503

HIGH PERFORMANCE COMPUTING

Mr. NATCHER. Doctor, how much are you requesting for high-performance computing in 1993 and how does that compare to your 1992 investment in this area?

Dr. WHITNEY. We are requesting $10,700,000 for 1993, which is an increase over the 1992 level of $9,800,000.

Mr. NATCHER. How do your activities in this field relate to the work of the Library of Medicine?

Dr. WHITNEY. Our computer emphasis is much different than the Library of Medicine. Theirs is in informatics—they use computers to distribute and collate information. Our computers are primarily to drive high technology research that requires computers to analyze complex structural biology problems and other kinds of problems that require complex computer support.

We also provide cross training to biologists in the area of computer science so we can get a better utilization of computers in the field of medicine.

RESOURCE CENTERS

Mr. NATCHER. As you know, Doctor, you have the largest number of centers at NIH, all of which are proposed for straight-line funding. Have you considered supporting fewer centers and giving inflationary increases to those that remain?

Dr. WHITNEY. Yes. We may have to support fewer centers because with a straight-line budget we will obviously not be able to make inflationary increases. There are going to be some hard choices. Throughout the years that has always been the situation: we support the centers that give us the biggest bang for the buck.

If we have to reduce the number of centers in order to make the rest succeed, we will do that.

GENERAL CLINICAL RESEARCH CENTERS

Mr. NATCHER. What are you doing to help the general clinical centers manage their cost during a funding freeze?

Dr. WHITNEY. A number of cost containment mechanisms have been introduced. The outpatient load has grown dramatically in proportion to the inpatient load because it is less expensive to do outpatient research than inpatient research. We have looked at cost sharing with the institutions on a case-by-case basis and have switched some GCRCs to per diem centers, which means we pay for beds only when they are occupied.

We have also been able to leverage some of the money for GCRCs by making sure that the institution or third-party carriers pay for their share of the use of the centers.

CHIMPANZEE BREEDING

Mr. NATCHER. How much are you spending on your chimpanzee breeding program and how many animals does it make available for research each year?

Dr. WHITNEY. We are requesting about $5,000,000 in 1993. We have a colony of about 480 animals, and we are producing just over 50 per year. Twenty-five of those would be returned to the colony, for breeding purposes, and twenty-five would be available for research.

AAALAC ACCREDITATION

Mr. NATCHER. What is the status of NIH's animal facility certification?

Dr. WHITNEY. We had a site visit by the American Association for Accreditation of Laboratory Animal Care for our intramural program in November of last year. Although we have not received written communication back from them, we anticipate receiving provisional accreditation. There is money in the 1993 budget to complete the AAALAC renovations that are required for the facilities to become accredited.

NONMAMMALIAN MODELS

Mr. NATCHER. How many new grants will you support in 1992 and 1993 for developing nonmammal alternatives for animal research?

Dr. WHITNEY. In 1992 and 1993 we will support about three new research project grants in this area.

Mr. NATCHER. How many applications did you receive in 1991 and how many did you fund?

Dr. WHITNEY. We received about 100 applications from our 1990 solicitation, and we funded 10 in 1990 and 12 in 1991.

Mr. NATCHER. What is the potential for developing computer and mathematical models as substitutes for animals in research?

Dr. WHITNEY. The use of the term "substitute" is somewhat misleading. I believe that mathematical modeling and computer modeling can be very helpful in perhaps reducing the numbers of animals and answering some questions earlier on that may not require the use of animals. Then we only need limited numbers of animals to verify the mathematical modeling.

We are supporting this year three mathematical and computer modeling project grants. It certainly has a place.

SHARED INSTRUMENTATION PROGRAM

Mr. NATCHER. What equipment is most frequently purchased through the shared instrumentation program?

Dr. WHITNEY. The shared instrumentation grant program supports a variety of what we call "big-ticket" items. They range from mass spectrometers to electron microscopes and nuclear magnetic resonance imagers. There are about a dozen different instrument types that are fairly well represented across the spectrum of the shared instrument grant program. Most of these instruments are in the $150,000 to $400,000 range. We only pay up to $400,000 for the instrument, although some of the NMR machines may cost as much as $1 million.

Mr. NATCHER. How do you ensure that institutions don't use equipment purchased with a shared instrumentation grant for nonresearch activities?

Dr. WHITNEY. It is a very competitive program. The application must cite the users' proposed use of the equipment; the grants they are using it on; and the time they are going to use it. That is a good portion of the criteria for judging the application. We average eight users per instrument awarded through the shared instrumentation grant program.

Mr. NATCHER. Mr. Pursell?

Mr. PURSELL. I have no further questions. Thank you.

Thank you, Dr. Whitney.

RESEARCH PROJECT GRANTS

Mr. NATCHER. Now, Doctor, how much equipment is purchased through regular research project grants?

Dr. WHITNEY. About 50 percent of the equipment that is purchased using NIH dollars is purchased through research project grants. However, this equipment is what I would call "small-ticket" items. The large expensive equipment that I just mentioned to you in the shared instrument grant program is not the kind that is bought through a research project grant. About 25 percent of NIH-supported equipment is bought through the shared instrument program and our biotechnology centers. Some equipment is also bought through the other extramural mechanisms.

Mr. NATCHER. Mr. Stokes, I yield.

MINORITY RESEARCH

Mr. STOKES. Just a couple of questions.

Doctor Whitney, can you describe for the Committee the resources and the funding levels which will be provided for minority-specific research activities in your Institute in fiscal year 1993?

Dr. WHITNEY. In 1993 there will be $45,832,000 for minority programs in the NCRR budget.

Mr. STOKES. How does that compare with fiscal year 1992?

Dr. WHITNEY. In 1992 there was $33,232,000. Most of the increase is the $12,000,000 in the Research Facility Improvement Program for HBCUs and other similar institutions. That is the major difference.

Mr. STOKES. Can you give us some idea of the extent to which you work with the Office of Minority Health under Dr. Ruffin?

Dr. WHITNEY. Dr. Ruffin has been very helpful to us. We have been developing a number of programs to entice minority entrants into our specialties and disciplines.

For example, we are developing a targeted minority program in the specialty of laboratory animal medicine and research in comparative medicine.

You are familiar with the Minority Clinical Associate Physician program in the general clinical research centers and the Science Teacher Education Program among others. We have discussed the Science Education Partnership Award, and have received some funding from Dr. Ruffin's office to help us with this effort.

Mr. STOKES. You are doing a good job, Dr. Whitney. Thank you very much.

Thank you, Mr. Chairman.

MINORITY CONSTRUCTION

Mr. NATCHER. Doctor, have you submitted authorizing legislation to Congress for your proposed facilities program for minority institutions?

Dr. WHITNEY. I understand the request is being prepared in the Department. We have applied, on several occasions, and continue to apply for general construction authorization.

Mr. NATCHER. How many construction grants would you expect to award?

Dr. WHITNEY. Ten to twelve with the $12,000,000.

Mr. NATCHER. Dr. Whitney, we want to thank you and your associates for appearing before our Committee on behalf of your budget request for fiscal 1993. It has been a good hearing, Doctor. We appreciate it.

Dr. WHITNEY. Thank you. We appreciate it also.

Mr. NATCHER. The Committee will now adjourn until 10:00 o'clock in the morning.

[The following questions were submitted to be answered for the record:]

RESEARCH CENTERS IN MINORITY INSTITUTIONS

Mr. Natcher: Identify the 17 institutions which receive Research Centers in Minority Institutions grants each year.

Dr. Whitney: The seventeen institutions that receive funding from the Research Centers in Minority Institutions program are as follows:

Atlanta University Graduate School
City College of New York
Hunter College
Charles R. Drew Postgraduate Medical School
Florida A&M School of Pharmacy
Howard University Medical School
Morehouse Medical School
Texas Southern University
University of Puerto Rico, San Juan
Tennessee State University
University of Hawaii
Universidad Central de Caribe
Xavier University of New Orleans
Meharry Medical School
Ponce School of Medicine, Puerto Rico
University of Puerto Rico, Rio Piedras
Tuskegee Institute

Mr. Natcher: On average, how much NIH grant funding do institutions with RCMI grants receive? Has this level increased over time by more than the biomedical research deflator?

Dr. Whitney: In 1980, before the RMCI program was initiated, the RCMI institutions received approximately $24 million in NIH grant funding. In 1991, they received approximately $69 million, including $22.1 million in RCMI funds. This is a greater increase than the biomedical research deflator.

MINORITY CONSTRUCTION

Mr. Natcher: Does your proposed funding for minority institutions facility construction require extended availability?

Dr. Whitney: Although extended availability of construction funds would be beneficial in managing this program, such availability is not required.

REGIONAL PRIMATE RESEARCH CENTERS

Mr. Natcher: How much NIH grant funding do the regional primate centers receive?

Dr. Whitney: In 1991, the Regional Primate Research Centers hosted NIH research totaling approximately $81 million, excluding NCRR support.

SHARED INSTRUMENTATION

Mr. Natcher: The Shared Instrumentation program represents what percentage of total NIH funding supporting extramural instrumentation?

Dr. Whitney: The Shared Instrumentation Grant program in 1991 provided approximately 22 percent of the total NIH funding for extramural instrumentation, and about 60 percent of instrumentation costing in excess of $100,000.

ANIMAL FACILITY IMPROVEMENT

Mr. Natcher: Provide a five-year table identifying the NIH investment in animal facility improvement, both extra- and intramural.

Dr. Whitney: Funding for animal facility improvement provided through the NCRR for the extramural community and provided through the Buildings and Facilities account for the NIH intramural program for the past five years is as follows:

	Extramural	Intramural
1989	$14,131,000	-0-
1990	13,931,000	$ 5,300,000
1991	13,839,000	18,146,000
1992	13,965,000	16,500,000
1993	13,965,000	10,500,000

BIOMEDICAL RESEARCH SUPPORT GRANTS

Mr. Natcher: Explain why the proposed appropriations bill language regarding overhead expenses is necessary.

Dr. Whitney: The general research support grants have never paid indirect costs on awards, because of the type of support they provide. The appropriation language has included a statement prohibiting such payments for many years in the past; in the 1992 bill, this language was inadvertently dropped. Restoration of the language would ensure that the traditional practice of not paying overhead costs on these grants would continue.

CLINICAL TRIALS

Mr. Natcher: Your budget documents indicate that you will support $56 million in clinical trials. What clinical trials does NCRR support directly?

Dr. Whitney: The NCRR does not support its own specific clinical trials. However, the General Clinical Research Centers provide the infrastructure of clinical beds, research nurses, nutritionists, diagnostics and other support which enable many of the clinical trials supported by the categorical Institutes to be carried out in a more cost effective manner.

RESEARCH CENTERS IN MINORITY INSTITUTIONS

Mr. Natcher: How many institutions receiving RCMI grants also participate in the MBRS or MARC programs?

Dr. Whitney: Sixteen of the seventeen RCMI grantees participate in the Minority Biomedical Research Support program. Twelve of the institutions also participate in the Minority Access to Research Careers program.

BIOLOGICAL MODELS AND MATERIALS RESEARCH

Mr. Natcher: Provide a breakout of your 1992 funding and 1993 Request for biological models and materials research by program and by mechanism.

Dr. Whitney: The Biological Models and Materials Research Program has no sub-program breaks. The funding by mechanism for this program is as follows:

	1992	1993
Research Project Grants	$3,986,000	$4,136,000
Research Centers	2,195,000	2,195,000
Other Research	1,168,000	1,168,000
Research Contracts	978,000	978,000
Total	$8,327,000	$8,477,000

COMPARATIVE MEDICINE

Mr. Natcher: Provide a breakout of your 1993 request for the Laboratory Animal Sciences program.

Dr. Whitney: The breakout of the 1993 request for the Comparative Medicine Program, formerly known as the Laboratory Animal Sciences and Primate Research Program, is as follows:

Research Project Grants	$ 3,841,000
Research Centers	52,671,000
Other Research	13,654,000
Research Training	2,666,000
Research Contracts	412,000
Total	$73,244,000

NCRR RESOURCES

Mr. Natcher: What is the total funding support from the Institutes for users of NCRR resources?

Dr. Whitney: The total extramural research support from the Institutes for users of NCRR resources was over $1 billion in 1991.

INTRAMURAL RESEARCH RESOURCES

Mr. Natcher: Identify obligations for NIH intramural research resources by activity for 1992 and 1993.

Dr. Whitney: Estimated obligations for the intramural research resources provided by the NCRR through the Management Fund and the Service and Supply Fund for 1992 and 1993 are as follows:

	1992	1993
Biomedical Engineering and Instrumentation	$24,033,000	$24,287,000
Veterinary Resources	36,912,000	35,323,000
Medical Arts and Photography	11,297,000	12,187,000
NIH Library	6,766,000	7,118,000
Total	$79,008,000	$78,915,000

GENERAL CLINICAL RESEARCH CENTERS

Mr. Natcher: How many of your general clinical centers are AIDS clinical trial units?

Dr. Whitney: Of the 28 new AIDS Clinical Trials Units to be funded in 1992, 26 are located at institutions with General Clinical Research Centers.

Mr. Natcher: How does the total patient caseload at your general clinical centers compare to the NIH clinical center?

Dr. Whitney: Data for both the General Clinical Research Centers and the NIH clinical center are as follows for FY 1990:

	GCRCs	NIH Clinical Center
Admissions	31,109	9,317
Inpatient Days	116,701	98,276
Outpatient Visits	202,477	150,934

Mr. Natcher: Are costs per patient comparable?

Dr. Whitney: The cost of the GCRC inpatient and outpatient activity, outlined above, was $112.2 million. The cost of the NIH clinical center activity was $173.0 million.

In contrast to the NIH clinical center, GCRC sites can build on infrastructure already in place at academic medical centers. As a result, considerable cost savings accrue. The NIH clinical center cannot use that approach.

SCIENCE EDUCATION

Mr. Natcher: Why does NCRR administer the Science Education Partnership Award program rather than the Office of Science Education within the Office of the Director?

Dr. Whitney: Funds for the Science Education Partnership Award are administered by the NCRR on behalf of the Office of the Director because the Office of the Director does not have the authority to make grant awards. This practice is similar to the way funds for the Research Centers in Minority Institutions were administered until the program became part of the NCRR budget in 1991.

Mr. Natcher: Your budget does not include funds for the Science Education program. Who provides this funding?

Dr. Whitney: The appropriation for the Office of the Director includes funding for the Science Education program.

ANIMAL FACILITY CERTIFICATION

Mr. Natcher: What share of NIH grantees meet animal facility certification standards?

Dr. Whitney: Prior to receiving an award, all NIH grantee institutions that will utilize animals in research must file a statement that they are in compliance with the PHS regulations governing research animal care. Further, every research protocol using animals is reviewed by the Institutional Animal Care and Use Committee prior to initiation.

BIOMEDICAL RESEARCH TECHNOLOGY

Mr. Natcher: Is there quite a bit of turnover among the Biomedical Research Technology centers, given the rapid changes in technology?

Dr. Whitney: Yes, approximately 10 percent of the centers funded by the Biomedical Research Technology program are turned over each year. These are largely replaced by resource centers in new technology areas.

SILVER SPRING MONKEYS

Mr. Natcher: Provide an update on the status and location of the remaining Silver Spring monkeys and indicate how many have been euthanized or died of natural causes. How does NIH plan to manage the care of the remaining monkeys?

Dr. Whitney: In June 1986, fifteen Silver Spring monkeys were transferred to the Tulane Regional Primate Research Center. In September 1987, five unoperated male cynomolgus monkeys were transferred to the San Diego Zoo.

At the present time, two monkeys are being cared for at the Tulane Center. One is an unoperated female rhesus that has been fully resocialized. The other is a surgically-disabled cynomolgus male. This animal is an amputee and presents formidable problems in veterinary care. The three monkeys at the San Diego Zoo have been fully resocialized.

Thus far, two of the monkeys at the Tulane Center have died of natural causes; six surgically disabled monkeys have been euthanized because veterinarians had determined their physical conditions had deteriorated significantly. Brain mapping studies were performed prior to euthanasia. Two monkeys at the San Diego Zoo have died of natural causes. A total of five animals remain at the two sites.

As promised, current plans call for the care and maintenance of the monkeys at each location. The deafferented monkey at the Tulane Center remains a unique source of data and will be studied only when veterinarians report that he is in severe distress or experiencing unrelievable chronic pain and should be euthanized for purely humane reasons.

GENERAL CLINICAL RESEARCH CENTERS

Mr. Stokes: The GCRC program supports a national network of clinical research facilities distributed within 30 states. For FY 1993, this program would be level-funded at $126.9 million. Information shared with my office suggests that shortfalls in the support of this program nationwide have led to the closure of nine programs in the last two years, in addition to program-wide funding cuts for those centers that continue to get support. What level of funding was requested by NCRR for this program? How much was approved by OMB?

Dr. Whitney: The NCRR requested $187,496,000 for the General Clinical Research Centers program in 1993. The President's budget request is $126,882,000.

Mr. Stokes: Under the President's budget, will any more centers have to be closed?

Dr. Whitney: The FY 1993 budget proposes to fund 74 GCRCs, the same number of centers as for FY 1992.

Mr. Stokes: What states do not have GCRC programs?

Dr. Whitney: The following states do not have GCRC programs located in them: Alaska, Arizona, Arkansas, Delaware, Hawaii, Idaho, Kansas, Maine, Mississippi, Montana, Nebraska, Nevada, New Hampshire, New Jersey, North Dakota, Oklahoma, Rhode Island, South Dakota, West Virginia and Wyoming.

Mr. Stokes: To what extent are these centers located in urban versus rural areas?

Dr. Whitney: Essentially all the centers are in urban areas within academic medical centers. The urban site populations vary considerably -- for example, Ann Arbor, Michigan; Charlottesville, Virginia; New York, New York. The referral base for patients at GCRC sites is local, regional and national, depending on the nature of the clinical research project and whether an unusual disease is undergoing study or novel therapy is under development. As a result, patients from urban, suburban and rural areas participate in the clinical research activities across the network of GCRCs.

Mr. Stokes: To what extent are these centers addressing minority health issues?

Dr. Whitney: The General Clinical Research Centers program is addressing minority health issues through several different mechanisms. GCRC investigators examine why Blacks have high blood pressure more commonly than non-Blacks, design effective ways of treating that high blood pressure, examine perinatal morbidity and mortality among minority populations. In 1991, approximately $16.7 million of GCRC funds were used to host minority-related research.

SHARED INSTRUMENTATION

Mr. Stokes: SIG Grants provide support for expensive state-of-the-art instruments utilized in both basic and clinical research. Applications are limited to instruments that cost at least $100,000 to $400,000. For FY 1993, the President proposes $8.8 million, the same as last year, but significantly less than the $32.7 million provided in FY 1992. To what extent has this program been cost effective?

Dr. Whitney: In order to provide real growth for the higher priority research project grants, and in light of the limits imposed by the Budget Enforcement Act, most other mechanisms were straightlined from FY 1992. The Shared Instrumentation Grant program has proven very cost effective, requiring as it does the sharing of this expensive equipment by at least three NIH-supported investigators. The average number of investigators using equipment purchased through the Shared Instrumentation Grant program is eight. This is the only program providing expensive instrumentation for NIH researchers.

Mr. Stokes: To what extent has last year's reduction hurt the program?

Dr. Whitney: The reduction in this program in 1992 was approximately 75 percent from the 1991 level. As a result, we were able to fund only about 36 awards, as compared with 139 in 1991. Since the application load is approximately the same (400 applications), the success rate has been reduced significantly, to 9 percent.

Mr. Stokes: Over the last six years, to what extent has there been an increase in the number of applications which have been submitted each year?

Dr. Whitney: Over the past six years, the number of applications submitted has increased from approximately 280 to about 400.

Mr. Stokes: How much did NCRR recommend for this program in FY 1993? How much was provided by OMB?

Dr. Whitney: The NCRR requested $48,437,000 for the Shared Instrumentation Grant program in its preliminary request to NIH. The President's budget request for this program is $8,758,000.

Mr. Stokes: To what extent is it possible that the cost of these types of instruments can be funded under R-01 grants?

Dr. Whitney: The instruments provided through the Shared Instrumentation Grants are too costly to be purchased through the usual research project grant mechanisms, without having a significant impact on the average cost of those awards. In 1991, $2.2 million for equipment costing in excess of $100,000 was funded through research project grants, approximately 4 percent of the total spent by NIH.

Mr. Stokes: To what extent have historically black colleges and universities benefitted from this program?

Dr. Whitney: In 1987, the Morehouse School of Medicine applied for and received two Shared Instrumentation Grant awards - one for a state-of-the-art electron microscope and the other for a digitized video image analysis system.

PRIMATE CENTERS

Mr. Stokes: The request includes $3 million to continue to address repair and renovation needs of the regional primate centers. How does this level of funding compare to the amount provided last year?

Dr. Whitney: A level of $3 million has been provided annually to address the repair and renovation needs of the Regional Primate Research Centers over the past several years.

Mr. Stokes: Is this the requested amount you submitted to the Department? How much did you request?

Dr. Whitney: The amount requested from the Department was $3 million. The amount requested in the preliminary budget request to NIH was $11 million.

Mr. Stokes: Do you have any data on what total level of funding is needed to address the repair and renovation needs of these centers?

Dr. Whitney: We estimate that between $35 million and $40 million will be required to meet the requirements of the new USDA regulations regarding primates.

Mr. Stokes: To what extent are animal welfare advocates causing damage to these centers?

Dr. Whitney: To date, damage to the Regional Primate Research Centers caused by animal welfare advocates is not significant.

MINORITY EFFORTS

Mr. Stokes: Dr. Whitney, you have been the director of NCRR since 1990, is that correct? And, before that you were acting director of the Division of Research Resources for approximately two years? During your tenure what efforts have you taken to promote minorities, particularly African Americans to the higher grade levels?

Dr. Whitney: The NCRR has a very active program to both recruit and promote minority employees. We are participants in the Federal Equal Opportunity Recruitment Program and have identified 20 occupational categories as targeted recruitment areas. Special recruitment activities are used to ensure that we attract minorities into the selection pool. For example, we advertise our vacancies in local and national newspapers, in the Affirmative Action Register, and in professional journals. We contact professional organizations and college alumni in the area. Our EEO office has direct contact with counsellors and program coordinators at schools and universities with high concentrations of minorities and women.

We encourage employee participation in upward mobility programs and provide opportunities for employees to grow and move up in the Center. In the last two years we have promoted 30 minority employees, including 10 who have moved into career ladder positions with promotion potential to the GS-12 level.

Mr. Stokes: To what extent are the RCMI institutions working in collaboration with this office?

Dr. Whitney: To date the RCMI grantee institutions have not participated in the Office of Minority Programs initiatives. However, the director of the RCMI program has been invited to take part in the Office of Minority Programs roundtable in order to plan for their participation.

BIOMEDICAL RESEARCH TECHNOLOGY PROGRAM

Mr. Early: Doctor, would you briefly discuss how technology development over the past several years has changed the nature of Basic Biomedical Research.

Dr. Whitney: Technology development has profoundly changed the nature of basic biomedical research, both in the explosion of new capabilities and in the increasing need for researchers to approach problem solving through multidisciplinary collaborations. Just a few examples follow.

Several areas of technology development have focused on enabling scientists to gain new insights into proteins, the building blocks of life. An understanding of protein structure, dynamics, and function is central to many biomedical research objectives.

The critical technology of genetic engineering has allowed, for the first time, the production of sufficient amounts of proteins to permit scientists to apply other newly emerging technologies to obtain in-depth molecular information. New methods of protein separation, purification, characterization, and visualization now permit investigators to achieve the goal of elucidating details about the structure and dynamics of proteins. An important example is the use of synchrotron radiation to yield the finest detail of atomic arrangements of crystalline molecules. This has allowed investigators to visualize the entire three-dimensional molecular structure of proteins and even intact viruses, which paves the way for rational drug design.

An important tool for characterizing proteins in their natural, non-crystallized state is nuclear magnetic resonance, which also permits studies of protein dynamics. Advances in computer technology and algorithm development have been critical in computation and interpretation of data derived from both of these methods.

Technology development in these and other areas has brought forth a new underlying principle of how biomedical research is conducted: today, more than ever, multidisciplinary approaches are essential to achieving research goals. Present research requires a level of skill and understanding of so many complex tools and techniques that it has become nearly impossible to proceed in any significant research project without expertise and collaboration across several fields.

Mr. Early: Over the past week, we've heard a great deal about the importance of structural biology and molecular biology and the exciting opportunities that they have opened up. Has NCRR's biomedical research technology program had an impact on the development of these fields?

Dr. Whitney: The Biomedical Research Technology program of the NCRR has had a major impact on research in the structural biology and molecular biology areas. The program funds resource centers at three existing U.S. synchrotrons for biomedical research scientists; these are the primary synchrotron access stations for NIH-supported scientists. The BRT program also supports high performance computing centers to analyze molecular biology data on proteins, viruses and nucleic acids, and supports an extensive group of instrument-based centers in areas including microscopy and spectroscopy serving the structural biology and molecular biology communities.

Mr. Early: How important is the development of new technologies to advances in biomedical science? Are they now more important?

Dr. Whitney: "The vision of a scientist is limited by his instruments" is a quote from the famous scientist Neils Bohr. Historically, progress in biomedical science has resulted from two types of events--from improvements in the techniques of observation, particularly with novel instruments and, quite independently, from conceptual changes permitting new interpretations of observations. Instrument and technology research has always been and will remain an important aspect of both of these events; thus progress in research and progress in technology are linked.

A recent NCRR workshop on structural biology reinforced this view by making it clear that conceptual changes have taken place regarding biological processes such as the immune response and gene regulation, and their connections with disease processes. Technology was the source of this new understanding, which is leading to yet more new ways to study health-related processes and structures.

Mr. Early: Do we need to continue to refine and to develop new technologies in order to maintain our leadership position and competitiveness in science?

Dr. Whitney: Although the U.S. remains at the forefront in many newly developing areas of technology, the continuing shortage of research funds for equipment and instrumentation development has had an adverse effect on our Nation's competitive edge. Many foreign laboratories are better equipped and many advanced instruments are made only in Europe or Japan. The U.S. must continue to develop and provide new technologies not only to maintain our competitiveness, but also to maintain progress in science.

BIOMEDICAL RESEARCH TECHNOLOGY

Mr. Early: Doctor, can you give us some idea of how long it takes to develop a new technology and applications of a new technology?

Dr. Whitney: The lifetime of an instrument at the frontier of science is about five to seven years; this is the time frame for improved instruments or technologies and applications to be developed. More profound changes occur when fundamentally new methods or technologies become available; this is a rarer event, and may take a decade or so to develop from concept to application, with a much lower success rate.

Mr. Early: Until this past year (FY 92), is it correct that support for the biomedical research technology program has been level since 1985 and has declined in terms of constant dollars?

Dr. Whitney: Yes, that is true.

Mr. Early: What impact has this had on the BRT program? What actions have centers had to take because of the constrained funding level?

Dr. Whitney: The level of funding has led to a decrease in the percentage of recommended costs we can award. New centers have to be equipped, and the added capital costs along with the increasing costs of biomedical technology inevitably lead to smaller numbers of centers. Existing centers also face restrictions in major equipment purchases since the demand far exceeds available funds. In most cases, centers have had to scale back both research and service activities. New services or capabilities have been especially hard hit.

Mr. Early: What impact does inadequate resources have on the BRT program's ability to support development of emerging technologies?

Dr. Whitney: The BRT program has begun funding research project grants over the past two years for the first time. These grants are primarily supporting new technologies and new instrument development. Technological research and development also remains a major focus of research support in BRT resources. The program support for emerging technologies remains strong except in cases where major capital equipment costs are involved.

Mr. Early: Doctor, will the FY 93 budget request allow you to provide increased support to existing BRT centers?

Dr. Whitney: Although there is a small increase in the Biomedical Research Technology centers program in 1993, that increase will provide for an additional center for high performance computing and communications. There are no funds for increased support to existing centers, and these centers will be funded at the 1992 level.

Mr. Early: Will they be able to implement needed expansions to accommodate new developments and outstanding opportunities?

Dr. Whitney: The centers will be able to expand only if other components are reduced. Outstanding opportunities will be pursued within center budgets, in order to keep the centers and their mission viable.

Mr. Early: Does the budget request include the necessary funding for new methodology development?

Dr. Whitney: No new funds are included for new methodology development; however, this activity is ongoing in the program and will continue in 1993 at approximately the same level as in 1992.

Mr. Early: Do you agree with the conclusion of a recent workshop on biomedical research technology that the nearly level funding has caused stagnation in developing new initiatives and effective utilization of existing facilities?

Dr. Whitney: Opportunities in molecular and structural biology have never been better, and both laboratory and shared equipment and facilities are needed to move to the next level in understanding biological processes and diseases. Limited budget increases in the Biomedical Research Technology Program have affected new activities in regional and national resource centers and facilities. Funds for additional staff and new equipment are often delayed or even eliminated, and expansion of activities into off-hours to address increased needs is often impossible. Utilization of these resources remains high, and new activities have mainly been affected by the late arrival of promised new instruments and methods for users.

Mr. Early: Doctor, in your professional judgement what should we be doing in this area?

Dr. Whitney: A funding level of $62.9 million in this program would provide for expansion in the areas of novel spectroscopies and microscopies, as well as providing additional support for the centers in the areas of synchrotrons, high performance computing and other high technology resources to meet the needs of NIH researchers.

Mr. Early: What was NCRR's original request for this program, and how does it differ from the request before us?

Dr. Whitney: The NCRR preliminary budget request to NIH for this program was $66,337,000, $20,017,000 more than the President's budget request.

Mr. Early: What priorities would NCRR pursue if additional resources were available for this program?

Dr. Whitney: If additional funds were available for this program, our most important priority would be to provide current services for the resource centers, plus two percent real growth (the same as for the research project grant program). We would provide funds for additional synchrotron resources, additional high performance computing centers, and expansion of research in novel spectroscopies and microscopies.

Mr. Early: I've read that a crisis is looming for many of the existing technologies that have provided important insights in structural and molecular biology. What can you tell us about this situation?

Dr. Whitney: NIH's decision to reduce support for technologies is evident in the decrease in support for shared instrumentation, the decrease in equipment funds available from research project grants and the relatively level budget for the Biomedical Research Technology program.

BRT RESEARCH TRAINING

Mr. Early: I understand that training across disciplines (engineering, computer science, and the physical and biological sciences) is crucial to the development of new biomedical research technologies. Is this correct?

Dr. Whitney: Yes, it is.

Mr. Early: What action is the NCRR taking to address this need?

Dr. Whitney: Cross-disciplinary training always has been an important feature of NCRR resource centers. Recently, NCRR has proposed to establish under the High Performance Computing and Communication initiative a formal multi-disciplinary training program. Initially this program will focus on providing training for postdoctoral bioscientists in computational techniques.

Mr. Early: Do we need to establish multi-disciplinary training grants to attract talented new students to biomedical research technology?

Dr. Whitney: The increasing technological complexity of biomedical research has greatly increased the need for researchers possessing expertise in both basic and technological sciences. Traditional training grants have not proven flexible enough to provide adequate levels of multi-disciplinary training. Training programs need to be specifically targeted to cross-training to meet this growing need.

Mr. Early: Are there any new initiatives and is there any new money in your budget request to address this area of need?

Dr. Whitney: In order to provide real growth to the highest priority, research project grants, there are no new funds requested to address this area of need.

Mr. Early: Doctor, according to your budget justification, NCRR will make no new institutional training awards in either FY 91, FY 92 or FY 93? Why is that and is this something that concerns you?

Dr. Whitney: The NCRR training program is entirely in the area of comparative medicine, training veterinarians in research. Any new applications must compete with renewal applications for funding, within the limited funds available.

GENERAL CLINICAL RESEARCH CENTERS

Mr. Early: For FY 93, the budget request proposes to level fund the general clinical research centers program at $126 million. What effect will this have on these centers?

Dr. Whitney: In order to provide real growth for the highest priority, research project grants, no increase is provided to the centers.

Mr. Early: Will they be able to support the same level of activity as in FY 92?

Dr. Whitney: Our 1993 request provides for 74 centers, the same number as 1992. Since the resource level is straightlined, centers must look for additional efficiencies.

Mr. Early: How much of its increased cost will each center be expected to absorb in FY 92 and FY 93?

Dr. Whitney: In 1993, on average, each center would have to absorb about six percent of its total budget relative to 1992, or all of its increased cost. The only alternative would be to close some centers in order to more fully fund the remainder.

Mr. Early How much did the cost of conducting clinical research increase in FY 91 and what are your projections for FY 92 and FY 93?

Dr. Whitney: The cost of supporting 74 centers in 1991, three fewer than in FY 1990, was $118,414,000, a 3.2 percent increase over FY 1990. In FY 1992, we will support 74 centers with $125,917,000. In FY 1993, in order to provide for real growth for the highest priority, research project grants, the request for centers is the same as 1992. The average salary for a research nurse increased by 21 percent in FY 1991. Nurses account for more than one-third of center costs. We expect nursing salaries to continue to increase at high rates. High quality research nurses are critical to the mission of the GCRCs.

Mr. Early: Doctor, what is the council ceiling for FY 92? What is the projected council ceiling for FY 93, and does that include indirect costs?

Dr. Whitney: The Council ceiling for 1992 for the General Clinical Research Centers is $140,672,000. The ceiling for 1993 is estimated at $149,000,000. Both these figures exclude indirect costs, which usually average about eight percent.

Mr. Early: How many research beds will be supported in FY 92 and FY 93, and how does this compare with prior years?

Dr. Whitney: We anticipate that there will be approximately 100,000 inpatient research days in FY 1992 and approximately 85,000-90,000 in FY 1993. We believe that patient research days are a more valid measure of the usage of the centers than research beds.

Mr. Early: To what extent are GCRCs able to meet the increasing demand for research beds and outpatient research facilities?

Dr. Whitney: In order to provide for real growth for the highest priority, research project grants, and because of the limitations imposed by the Budget Enforcement Act, most other research mechanisms are straightlined in 1993. Because the budget for the GCRCs is the same in 1993 as in 1992, their ability to meet the increasing demand for research beds and outpatient days will be diminished. In an effort to meet the increased demand we have been modifying centers. Because outpatient research is more cost-effective and new research tools facilitate addressing clinical research questions in an outpatient facility, progressively more research is being done in that setting. Using GCRC funds, several centers have modified their physical facilities to accommodate more outpatient-based research. Outpatient studies can now be carried out in specially adapted and staffed facilities for up to 10-12 hours. Because of cost constraints, inpatient research is conducted intensively, whenever possible, over fewer days.

Mr. Early: Do you expect AIDS related research at GCRCs to continue to increase?

Dr. Whitney: Yes. The number of HIV infected individuals continues to increase with progressively more pediatric cases because of the increasing number of women infected in the reproductive age group. Of the 28 AIDS Clinical Trial Units (ACTUs) to be funded later this year 26 are at GCRC sites. Multiple GCRCs will be used for the AIDS-related research activity at ACTUs.

Mr. Early: Do you expect the rapidly developing area of gene therapy research to place increased demands on the general clinical research centers?

Dr. Whitney: Yes. At least two different GCRC sites will begin gene therapy this fiscal year and several others will join them over the next few years. This is a new area for GCRCs and will require reconfiguration of existing resources and provision of additional resources because of the unique needs for several forms of gene therapy. Because gene therapy is experimental, GCRCs are poised to facilitate gene therapy research and assure that the rapid advances in biotechnology reach patients and become part of standard medical practice.

Mr. Early: What did NCRR request for the general clinical research centers program, and how does it differ from the request before us?

Dr. Whitney: The NCRR preliminary budget request to NIH for the General Clinical Research Centers was $187,496,000, $60,614,000 more than the President's budget request.

Mr. Early: The budget request states that the new opportunities for FY 92 and beyond exist in the rapidly developing areas of structural biology and molecular medicine. Highlight the most promising and tell us why they are important.

Dr. Whitney: The rapidly developing areas of structural biology will permit investigators to customize and speed up the development of "designer" proteins and other substances to treat or prevent several disorders, including high blood pressure, viral diseases such as HIV infection, cancers, and drug addiction. Structure-based drug design will result in novel treatments of disease, including some for which no adequate therapy exists. Those candidate therapies have to be tested in well-controlled clinical research settings before they become part of standard medical practice. Initiatives to be included with molecular medicine are already ongoing at GCRCs but will be greatly expanded to match the basic science advances and opportunities within this area.

Basic research tools are at hand now to define molecular mechanisms of disease as well as to design and test novel therapies. For example, a disorder may be attributed to a missing or abnormal enzyme linked to a single gene defect found in one of the approximately 5,000 genetic diseases. Collectively those genetic disorders affect 10-20 million Americans. Several different approaches can be used to correct the genetic abnormality -- replace the missing enzyme with a genetically-engineered protein, replace or repair the abnormal gene, or circumvent the abnormality with specific nutrients (biotin, for example), if possible. Novel forms of gene and related molecular therapies will be used to diagnose, prevent or treat cancers, drug addiction, cardiovascular and pulmonary diseases, and neurodegenerative disorders. Clinical research is central to assuring that the exciting advances within structural biology, biotechnology, and molecular medicine are translated to the bedside to assure that scientific advances impact positively on the health of the people of our Nation.

Mr. Early: What was NCRR's request for this program?

Dr. Whitney: NCRR's request to NIH for the GCRC program was $187 million for FY 1993. Biotechnology (which includes molecular medicine) and clinical trials each account for almost one-quarter of all GCRC research projects.

Mr. Early: What priorities would NCRR pursue if additional resources were available for this program?

Dr. Whitney: The NCRR would first support additional funds in this program to meet the requirements of current services plus a two percent increase to relink the centers with the NIH research project grant level of increase. We would like to fund three additional centers, initiate a program of clinical fellowships and career development, and expand the clinical associate physician program and collaboration with the Research Centers in Minority Institutions program. Funds are also needed for alteration and renovation to support expansion of research in gene therapy, molecular medicine, and pediatric AIDS.

PRIMATE CENTERS

Mr. Early: How much is available in your FY 93 budget request for core support for the primate centers, and how does this compare with FY 92 and FY 91 levels of support?

Dr. Whitney: The budget request for core support for the Regional Primate Research Centers is $28,045,000. The actual amount for this program in 1991 was $24,955,000, and in 1992 we estimate that $28,145,000 will be awarded for core support.

Mr. Early: How much did NCRR request for core support of primate centers and for repair and renovation of the centers?

Dr. Whitney: The NCRR preliminary budget request to NIH for core support of the Regional Primate Research Centers was $39.5 million, and $11 million was requested for repair and renovation of the centers.

ANIMAL FACILITIES IMPROVEMENT GRANTS

Mr. Early: What is your request for the extramural animal facilities improvement program? How many applications do you anticipate receiving and funding in FY 92 and FY 93?

Dr. Whitney: The President's budget request for the extramural animal facility improvement program is $10,965,000. We expect to receive approximately 80 applications and to fund approximately 45 awards in both 1992 and 1993.

Mr. Early: Is there still a backlog of approved but unfunded applications?

Dr. Whitney: Yes, there are still unfunded applications.

COMPARATIVE MEDICINE

Mr. Early: Why does NCRR plan to phase out support for diagnostic and investigative laboratories and to replace these awards with comparative medicine research program projects?

Dr. Whitney: In spite of the success of the diagnostic and investigative laboratories, we believe that scarce funds can be better used when focussed on research problems and opportunities. This is what the new Comparative Medicine Research program project awards will do. Many institutions have begun to pay for necessary diagnostic and quality control services through other means (chargeback, per diem charges, etc.). Accordingly we are now emphasizing support for needed research. The program projects are likely to provide the broadest, best and most long lasting investment value. Research supported by these projects will focus on such areas as the creation, production, maintenance, and preservation of genetically designed animals and further investigations into the etiology, pathogenesis, control and prevention of laboratory animal diseases or problems that adversely affect biomedical research or laboratory animal well-being. The projects should attract a broad variety of new investigational talent to research opportunities and needs in this area.

NCRR PRIORITIES

Mr. Early: If an increase over the FY 93 request is provided for NCRR, how would you use these additional funds? What would your priorities be?

Dr. Whitney: Like most areas of science, opportunities far outstrip the available resources. This challenges us to support the best and highest priority proposals. If additional funds were available, the NCRR would support research and development activities which are critical to biomedical research. Our highest priority is providing additional support to our resource center programs to continue our funding linkage to the research project grant mechanism: for the General Clinical Research Centers this would require an additional $7.2 million; for the Biomedical Research Technology resource centers, an additional $2.3 million; and for the Regional Primate Research Centers, an additional $2.3 million. This total of $11.8 million would continue resource center support to research project grantees at the 1992 level. Our next highest priority is to add another $2.8 million to resource centers to provide them with the same growth rate as was provided for research project grants. Hence, a total of $14.6 million would be required to relink NCRR resource center support with the research project grants the centers support.

Next we would restore the Shared Instrumentation Grant program to its 1991 level plus inflation, which would require $27.8 million. Such an addition would restore this unique program to its historic role as a provider of approximately one-fifth of all equipment to NIH grantees and about 60 percent of all equipment costing in the range of $100,000 to $400,000 to those grantees. These large, expensive and complex instruments are not readily provided through the individual research project grant mechanism.

Our next priority would be the addition of $15.8 million for research projects grants, to develop novel spectroscopies and micro-spectroscopies, as well as to emphasize the development of transgenic animal models, to undertake genetic and reproductive studies, to accelerate our work in development of new animal models for use in the study of AIDS and other problems in immunology, and to increase our efforts to develop non-mammalian models, particularly marine models.

Our next priority is in the area of human resource development focusing particularly on under-represented minorities in biomedical research. An additional $6.5 million would enable NCRR to expand its career development activities for minority clinical associate physicians, as well as research training and career development for the veterinarians and scientists working in laboratory animal science and medicine. The focus would be toward attracting under-represented minorities into these fields. The increase would also enable expansion of collaboration between the Research Centers in Minority Institutions medical schools and the General Clinical Research Centers, to increase the number of under-represented minorities both involved in clinical research and participating in clinical trials. An additional $7.5 million and two FTEs would enable NCRR to increase funding for the Science Teacher Enhancement Award Program and to expand the Science Education Partnership Award program.

Finally, we would like to initiate a small intramural research program which would focus primarily on high performance computing and communications, diagnostic imaging, and expansion of our research in the development of transgenic animal models. This initiative would require $3 million and an estimated 25 FTEs.

Mr. Early: Will any significant new research initiatives or opportunities be lost or delayed by lack of funds in the FY 93 budget?

Dr. Whitney: Like most areas of science, opportunities far outstrip the available resources. This challenges us to support the best and highest priority proposals.

Mr. Early: Please provide, for the record, a list of these along with brief descriptions and the funding requirements associated with each.

Dr. Whitney: The list follows:

An estimated $14.6 million could be used to fund NCRR resource centers at the same growth rate as NIH research project grants in 1993. An additional $27.8 million would be used to fund Shared Instrumentation Grants at a level which would be comparable to the 1991 actual obligations for these grants.

A number of research opportunities to develop marine models of human diseases as research resources could be undertaken as could research into and development of new high technologies such as micro-spectroscopies for structural biology research, development of new animal models for AIDS and other research, etc. An estimated $15.8 million would provide resources to undertake 80 new research projects in these promising areas. In addition, we could undertake a small but potent intramural research program in high performance computing, diagnostic imaging, and development of additional transgenic animal models with an additional $3 million and 25 FTEs.

Approximately $14 million could be used to (1) expand NCRR training and career development opportunities targeted to minorities; (2) initiate a program of clinical fellowships and career development, and a multidisciplinary biotechnology/high performance computing cross-training program; (3) accelerate the collaboration between the General Clinical Research Centers and the Research Centers in Minority Institutions; and (4) fully implement the Science Teacher Enhancement Award Program and the Science Education Partnership Award program, each of which is intended to extend the interest and capability of students and their science teachers in biomedical research and to attract those students to biomedical research careers.

Mr. Early: What impact is limiting the average increase in cost per award having on NCRR, particularly with respect to your research centers program?

Dr. Whitney: The limitation in average cost increase per award is having little effect on the research resource centers program, since we have always made it a practice to look carefully at each award to save whatever funds may be possible, and to make the centers as cost effective as possible.

SCIENCE TEACHER ENHANCEMENT AWARD PROGRAM

Mr. Pursell: What is the Science Teacher Enhancement Award Program and why is this program important?

Dr. Whitney: The NCRR will pilot a 24-month program using funds from the NIH Office of the Director. Its objective is to increase the number of lead middle, junior, and senior high school science teachers who are motivated to become involved in research projects to update their knowledge about science. Their involvement should enhance their instructional skill and their scientific knowledge so that current concepts in health science can be integrated into their teaching of students. Meeting this objective is very important to the future of the United States economy and its competitive posture in the World. We must improve our students' performance in science and mathematics, and we believe this is one way to approach that goal.

GENERAL CLINICAL RESEARCH CENTERS

Mr. Pursell: What is the relationship between the AIDS research activity of other parts of NIH and the General Clinical Research Centers?

Dr. Whitney: In 1986, 44 AIDS research projects funded by other NIH components were conducted at 20 General Clinical Research Centers, with a total value of less than $2 million. In 1991, by comparison, the number of projects had increased eightfold. AIDS research is now conducted at 59 of the GCRCs. Most of these research projects provide support for clinical trials of new drugs to prevent AIDS or to restore immune function. Other studies focus on new treatments for complications of AIDS in both adults and children.

Mr. Pursell: How are the GCRCs addressing minority health issues?

Dr. Whitney: There are two particular initiatives in the GCRC program which will impact on minority health issues. In 1991, the program expanded its Clinical Associate Physician Program to emphasize training for minority clinical associate physicians. The program will assist minority physicians and dentists to develop independent clinical research careers and provide a mechanism to attract those minority researchers to remain in research.

The GCRC program has also undertaken a major collaboration with the Research Centers in Minority Institutions medical schools, designed to increase the numbers of minorities participating in clinical trials and to develop and increase the number of minority clinical investigators, by developing satellites of funded GCRCs at minority institutions.

In addition, GCRCs support extensive research on diseases which disproportionately affect minorities, for example, hypertension, cancer, and infant mortality.

SHARED INSTRUMENTATION

Mr. Pursell: How much of NIH support for equipment in the extramural community is provided through the Shared Instrumentation Grant Program?

Dr. Whitney: Over the period from 1985 to 1991, the Shared Instrumentation Grant program provided approximately 22 percent of the total grant dollars awarded for equipment by the NIH. With the large decrease in the program in 1992, we cannot estimate the proportionate share these grants will support.

BIOMEDICAL RESEARCH SUPPORT GRANTS

Mr. Pursell: Describe for the committee the new Biomedical Research Support Grant Program.

Dr. Whitney: The Biomedical Research Support Grant program has been redesigned in order to meet some of the needs of the former program within the smaller budget available for the BRSGs in 1992 and 1993, approximately $5.2 million. Awards of $50,000 each will be made to 104 institutions, distributed evenly among the top third, middle third and lower third of institutions ranked on the basis of total BRSG funds awarded to the institution in 1991. The awards will be determined by competitive administrative review of applications by a trans-NIH panel, based on the impact of BRSG funds in previous years, the projected purpose for which the requested funds would be used, and the level of institutional commitment as indicated by matching contributions.

ANIMAL MODELS

Mr. Pursell: What is NCRR doing to find non-human primate animal models of HIV infection which could reduce the use of chimpanzees in this kind of research?

Dr. Whitney: The NCRR has pursued a vigorous program to breed chimpanzees for use in AIDS research, and research on hepatitis and other serious human diseases, in order to ensure the availability of this model for vaccine research. The use of the SIV model in monkeys has reduced the need for chimpanzees, and recently, a monkey called the Pigtailed Macaque has been discovered to be susceptible to both HIV-1 and HIV-2, the first non-human primate other than the chimpanzee to do so. This macaque represents an excellent animal model system that will permit the testing of candidate AIDS vaccines and the development of therapeutic drugs, and may further reduce the requirements for chimpanzees in this research.

INTRAMURAL RESEARCH RESOURCES

Mr. Pursell: How does the work of NCRR's intramural programs in Biomedical Engineering and Instrumentation and Veterinary Resources relate to the work supported through NCRR's extramural program?

Dr. Whitney: Both of these intramural programs are presently supported through the NIH Management Fund rather than through our appropriation. Each program provides a combination of research in collaboration with institute-supported investigators, independent research, and direct services to the NIH intramural program. In both the collaborative and independent research arenas, much the same as in the parallel extramural activities, engineering scientists and veterinary scientists are working on research problems whose solutions will yield significantly improved engineering as well as veterinary resources. The work of these two intramural programs is similar to that of corresponding programs in the extramural activity of the NCRR.

AIDS RESEARCH

Mr. Pursell: How does the NCRR AIDS program relate to those AIDS research programs of the institutes?

Dr. Whitney: The NCRR AIDS research program, the third largest at the NIH, consists primarily of two major components. The first provides substantial support for clinical AIDS research through our General Clinical Research Centers. These centers are the host sites for all but nine of the 47 AIDS clinical trials groups which are supported by the National Institute of Allergy and Infectious Diseases. NCRR funds in 1991 supported nearly 350 research activities at the 59 centers that hosted AIDS research, supporting nursing, dietary, computing, and other costs related to the clinical research effort.

The other major component is research conducted in and supported by our Comparative Medicine program. Some of the support relates to breeding and research programs involving chimpanzees and specific pathogen free Rhesus monkeys, as well as research on vaccine development. Approximately one third of the Regional Primate Research Centers' budget is for AIDS-related research. Other components of the NCRR have growing involvement in AIDS research activity as well, particularly the Research Centers in Minority Institutions, which are becoming more involved in encouraging minority participation in AIDS clinical trials.

SYNCHROTRON FACILITIES

Mr. Pursell: I understand that U.S. scientists have to travel to Europe and Japan to use synchrotron beamlines. Please tell us about NCRR's support for NIH scientists' access to synchrotron research facilities.

Dr. Whitney: NCRR presently supports biomedical researchers' use of synchrotron resources at three national research facilities. Utilizing funds provided by the Congress in 1992, we will be working with the Department of Energy to develop a fourth synchrotron resource for use by biomedical researchers. That facility will not be on line until 1995.

GENERAL CLINICAL RESEARCH CENTERS

Mr. Pursell: To what extent are the GCRCs involved in critical technology such as gene therapy?

Dr. Whitney: The GCRCs will be the major NIH-supported extramural sites for gene therapy. The University of Michigan has two gene therapy projects which have been approved by the NIH Recombinant DNA Committee. Gene therapy will be initiated for both in the spring or early summer of this year. Two other GCRC sites are close behind. Several other GCRC sites will be positioned to participate in gene therapy projects within the next 12-18 months and have submitted requests for support for that clinical research activity.

BIOTECHNOLOGY

Mr. Pursell: What is your Center doing to assure that important technologies for biomedical research are made available to biomedical investigators?

Dr. Whitney: Two of NCRR's programs highlight our actions to assure that biomedical researchers have access to state-of-the-art technologies. The Biomedical Research Technology program supports a variety of technology such as synchrotron X-ray sources, high performance computing centers, and image analysis centers. In addition to assuring the availability of the technology, the centers provide for training of research scientists in the use of the technology, for development of new applications, and for research and collaboration with biomedical investigators.

The Shared Instrumentation Grant program provides for the purchase of high technology instruments, in the cost range of $100,000 to $400,000, for use by groups of investigators at institutions across the country. These kinds of equipment range from nuclear magnetic resonance imagers and mass spectrometers to scanning laser confocal microscopes and gene sequencing devices.

BIOLOGICAL MODELS AND MATERIALS RESEARCH

Mr. Pursell: To what extent will your 1993 request support the development of resource centers in the Biological Models and Materials Research Program? What was your request to NIH for 1993 for this program?

Dr. Whitney: In order to provide real growth to the highest priority, research project grants, and in light of limits on growth by the Budget Enforcement Act, most other mechanisms were straightlined from FY 1992. The request for 1993 for the Biological Models and Materials Research program includes support for six research centers. No additional centers can be started in 1993. The 1993 preliminary budget request to NIH for this program was $30,225,000.

LINKAGE TO RESEARCH PROJECT GRANTS

Mr. Pursell: The request for Research Project Grants (RPG) continues to increase this year in the same way that it has for the past several years, yet the request for research resources, and especially resource centers and shared instrument grants, does not increase this year. How will these resources provide the infrastructure and support required for an increased number RPGs?

Dr. Whitney: In order to provide real growth to research project grants, the highest priority, resource centers in NCRR have not received increases commensurate with research project grants and total NIH budget increases.

HIGH PERFORMANCE COMPUTING AND COMMUNICATIONS

Mr. Pursell: What role does NCRR play in high performance computing and communications?

Dr. Whitney: The President's Office of Science and Technology Policy, through the Federal Coordinating Council on Science, Engineering, and Technology, has initiated a Subcommittee on High Performance Computing and Information Technology, a multi-agency high performance computing and communications program, to strengthen the Nation's research computing enterprise. NCRR is one of four NIH components collaborating in the effort to mount this program.

NCRR's investment in high performance computing and communications will be $10.7 million in 1993, supporting two new and two ongoing high performance computing centers. These activities include the development of innovative algorithms for use on state-of-the-art massively parallel processing architectures to solve several of the Grand Challenges described in the FY 1993 Subcommittee report. Studies will focus on theoretical simulation of biological systems using a multi-disciplinary approach to include the fields of quantum chemistry, statistical mechanics, molecular modelling, and biophysical theory. Some applications include protein folding, rational drug design, image processing data in real time from several different imaging technologies. As biotechnologies have enhanced sensitivities, computation requirements can only be addressed with new algorithms with advanced computer architecture.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Center for Research Resources

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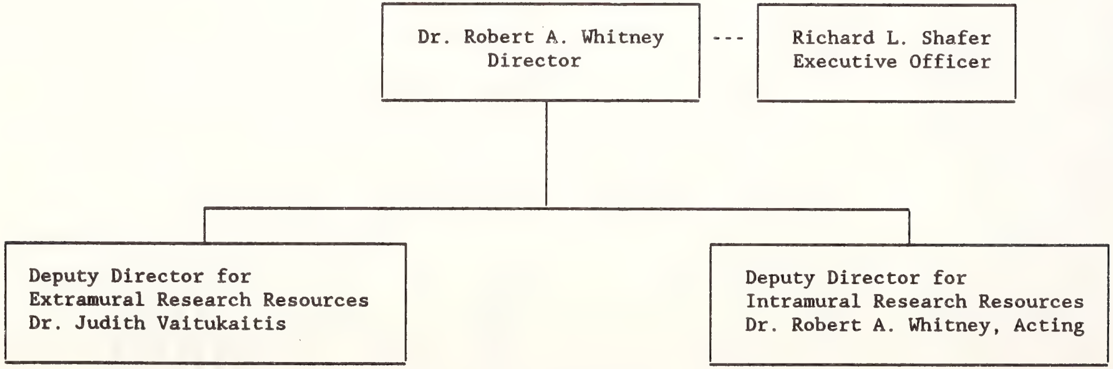
Organization Structure



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For carrying out section 301 and Title IV of the Public Health Service Act with respect to research resources and general research support grants, [$315,220,000] *$330,231,000, Provided, That none of these funds shall be used to pay recipients of the general research support grants program any amount for overhead expenses in connection with such grants,* Provided further, That of the funds made available under this heading, [$15,000,000] *$15,144,000,* shall not become available for obligation until September 30, [1992] *1993*.

(Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 1992.)

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Language Analysis

Language Provision	Explanation
"...Provided further, That none of these funds shall be used to pay recipients of the general research support grants program any amount for overhead expenses in connection with such grants."	To restore language included in appropriations acts from FY 1968 to FY 1991, prohibiting the payment of indirect costs to recipients of general research support grants.

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Amounts Available for Obligation 1/

	1991 Actual	1992 Appropriation	1993 Estimate
Appropriation...............	$343,796,000	$315,220,000	$330,231,000
Sequester Order.............	-4,000		
Section 514 (a) reduction...	-255,000		
Section 514 (b) reduction...	-8,286,000		
Section 214 reduction.......	---	-39,000	---
Section 513 (a) travel reduction.................		-64,000	
Section 513 (a) S & E reduction................	---	-566,000	---
Subtotal, adjusted appropriation...........	335,251,000	314,551,000	330,231,000
Real transfer from:			
NHLBI for SEPA	+555,000	---	---
Subtotal, adjusted budget authority..............	335,806,000	314,551,000	330,231,000
Unobligated balance brought forward..................	+59,000	+58,000	---
Unobligated balance available end of year.....	-58,000	---	---
Unobligated balance, lapsing..................	-31,000	---	---
Total, obligations........	335,776,000	314,609,000	330,231,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: FY 1991 -- $2,763,000; and FY 1992 -- $3,885,000; and FY 1993 -- $4,000,000.

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Budget Mechanism
(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	No.	Amount	No.	Amount	No.	Amount
Research grants:						
Research projects:						
Noncompeting	33	$6,009	41	$7,142	52	$8,974
Admin. suppl	(2)	36				
Competing						
Renewal	6	1,319	12	2,744	14	3,092
New	32	3,369	14	1,272	13	1,231
Supplemental	--	---	--	---	--	---
Subtotal competing	38	4,688	26	4,016	27	4,323
Subtotal, res. proj	71	10,733	67	11,158	79	13,297
Research Centers:						
Clinical research	74	117,048	74	125,963	74	125,963
Biomedical research technology	62	33,655	62	39,602	63	40,475
Comparative medicine program	41	48,536	41	52,671	41	52,671
Biological models and materials research	4	417	6	2,195	6	2,195
Research centers in minority institutions	17	22,090	17	23,574	17	23,574
Subtotal, research centers	198	221,746	200	244,005	201	244,878

Other research:						
Research career programs.........	11	795	11	796	11	796
Biomedical research support......	767	63,143	140	22,862	140	22,862
Other research related...........	94	19,314	88	16,075	88	16,075
Subtotal, other research.....	872	83,252	239	39,733	239	39,733
Total, research grants............	1,141	315,731	506	294,896	519	297,908
Training:						
Individual awards:						
Noncompeting..................	5	160	4	132	4	132
Competing:						
New.........................	--	---	2	60	2	60
Subtotal, individual.............	5	160	6	192	6	192
Institutional awards:						
Noncompeting..................	70	2,335	63	2,084	63	2,084
Competing:						
Renewal.....................	7	171	13	390	13	390
New.........................	--	---	--	---	--	---
Subtotal, institutional..........	77	2,506	76	2,474	76	2,474
Total, training..................	82	2,666	82	2,666	82	2,666
Research and development contracts	8	4,016	7	3,350	7	3,350
Facilities construction...........		---		---		12,000
	FTEs		FTEs		FTEs	
Research management and support.........................	98	13,393	97	13,639	97	14,307
Total............................	98	335,806	97	314,551	97	330,231
Clinical Trials................		(53,009)		(56,353)		(56,353)

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CROSSWALK - 1991 Actual
(Dollars in thousands)

	MECHANISM								
	Research Grants			Training Programs		Research and Development Contracts	Research Management and Support	Extramural Facilities	Total
PROGRAM ACTIVITY	Research Projects	Research Centers	Other Research	Indiv.	Instit.				
Clinical research....	$ 50	$117,048	$781			$565			$118,444
Biomedical research technology..........	3,780	33,655	1,924			1,523			40,882
Comparative medicine............	3,325	48,536	13,390	$160	$2,506	564			68,481
Biomedical research support.............			64,458						64,458
Biological models and materials research..	3,578	417	2,699			1,364			8,058
Research centers in minority institutions		22,090							22,090
Research facilities improvement.........									
Research management and support.........							$13,393		13,393
Total.........	10,733	221,746	83,252	160	2,506	4,016	13,393		335,806

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CROSSWALK - 1992 Appropriation
(Dollars in thousands)

	MECHANISM								
	Research Grants			Training Programs					
PROGRAM ACTIVITY	Research Projects	Research Centers	Other Research	Indiv.	Instit.	Research and Development Contracts	Research Management and Support	Extramural Facilities	Total
Clinical research....	$ 50	$125,963	$647			$222			$126,882
Biomedical research technology..........	3,578	39,602	1,402			1,738			46,320
Comparative medicine............	3,544	52,671	13,654	$192	$2,474	412			72,947
Biomedical research support.............			22,862						22,862
Biological models and materials research..	3,986	2,195	1,168			978			8,327
Research centers in minority institutions		23,574							23,574
Research facilities improvement.........									
Research management and support.........							$13,639		13,639
Total..........	11,158	244,005	39,733	192	2,474	3,350	13,639		314,551

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CROSSWALK - 1993 Estimate
(Dollars in thousands)

PROGRAM ACTIVITY	MECHANISM: Research Grants: Research Projects	Research Grants: Research Centers	Research Grants: Other Research	Training Programs: Indiv.	Training Programs: Instit.	Research and Development Contracts	Research Management and Support	Extramural Facilities	Total
Clinical research....	$ 50	$125,963	$647			$222			$126,882
Biomedical research technology..........	5,270	40,475	1,402			1,738			48,885
Comparative medicine...........	3,841	52,671	13,654	$192	$2,474	412			73,244
Biomedical research support............			22,862						22,862
Biological models and materials research..	4,136	2,195	1,168			978			8,477
Research centers in minority institutions		23,574							23,574
Research facilities improvement.........								$12,000	12,000
Research management and support.........							$14,307		14,307
Total.........	13,297	244,878	39,733	192	2,474	3,350	14,307	12,000	330,231

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Summary of Changes

1992 Estimated budget authority	$314,551,000
1993 Estimated budget authority	330,231,000
Net change	+15,680,000

	1992 Current Estimate Base		Change from Base	
	Pos. (FTE)	Budget Authority	Pos. (FTE)	Budget Authority
Changes:				
A. Built-in:				
1. Within grade increases	---	$5,605,000	---	+$47,000
2. Annualization of 1992 pay raise	---	5,605,000	---	+59,000
3. One less day of pay	---	5,605,000	---	-22,000
4. Payment for centrally furnished services	---	3,396,000	---	+235,000
5. Service and supply fund	---	1,100,000	---	+49,000
6. Increased costs of laboratory materials and other supplies	---	3,307,000	---	+141,000
7. DHHS Working Capital Fund	---	227,000	---	+16,000
8. FY 1993 pay raise	---	5,605,000	---	+158,000
Subtotal			---	+683,000
B. Program:	No.	Amount	No.	Amount
1. Research project grants:				
a. Noncompeting	41	7,142,000	+11	+1,832,000
b. Competing	26	4,016,000	+1	+307,000
Total	67	11,158,000	+12	+2,139,000
2. Research centers	200	244,005,000	+1	+873,000
3. Extramural facilities	---	---	---	+12,000,000
	FTEs		FTEs	
4. Research Management and Support:	97	13,639,000	---	-15,000
Subtotal				+14,997,000
Total changes				+15,680,000

NATIONAL INSTITUTES OF HEALTH

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Budget Authority by Activity

(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	FTEs	Amount	FTEs	Amount	FTEs	Amount
Clinical research..........	--	$118,444	--	$126,882	--	$126,882
Biomedical research technology...............	--	40,882	--	46,320	--	48,885
Comparative medicine program.................	--	68,481	--	72,947	--	73,244
Biomedical research support.................	--	64,458	--	22,862	--	22,862
Biological models and materials research.......	--	8,058	--	8,327	--	8,477
Research centers in minority institutions....	--	22,090	--	23,574	--	23,574
search facilities improvement.............	--	---	--	58	--	12,000
Research management and support.................	98	13,362	97	13,639	97	14,307
Subtotal, obligations....	98	335,775	97	314,609	97	330,231
Unobligated balances brought forward..........	--	-59	--	-58	--	---
Unobligated balance available end of year....	--	+58	--	---	--	---
Unobligated balance lapsing.................	--	+32	--	---	--	---
Total, budget authority..		335,806		314,551		330,231
HIV/AIDS	(11)	(47,429)	(11)	(50,036)	(11)	(51,505)

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Budget Authority by Object

	1992 Appropriation	1993 Estimate	Increase or Decrease
Total number of full-time permanent positions	93	93	---
Total compensable work years:			
Full-time equivalent employment	97	97	---
Full-time equivalent of overtime and holiday hours	2	2	---
Average ES salary	$124,000	$124,000	---
Average GM/GS grade	9.9	9.9	---
Average GM/GS salary	$40,730	$40,730	---
Average salary, grades established by act of July 1, 1944 (42 U.S.C. 207)	$77,607	$77,607	---
Personnel compensation:			
Full-time permanent	$4,305,000	$4,501,000	+196,000
Other than full-time permanent	229,000	246,000	+17,000
Other personnel compensation	151,000	162,000	+11,000
Total, personnel compensation	4,685,000	4,909,000	+224,000
Personnel benefits	920,000	987,000	+67,000
Benefits for former personnel	4,000	4,000	---
Travel and transportation of persons	141,000	194,000	+53,000
Transportation of things	36,000	39,000	+3,000

	1992 Appropriation	1993 Estimate	Increase or Decrease
Rent, communications, and utilities.	254,000	261,000	+7,000
Printing and reproduction..........	178,000	185,000	+7,000
Other services:			
Project contracts................	3,350,000	3,350,000	---
Centrally furnished services......	3,396,000	3,631,000	+235,000
Other............................	3,791,000	3,818,000	+27,000
Supplies and materials............	109,000	119,000	+10,000
Equipment.........................	125,000	160,000	+35,000
Grants, subsidies & contributions...	297,562,000	312,574,000	+15,012,000
Total............................	314,551,000	330,231,000	+15,680,000

NATIONAL INSTITUTES OF HEALTH

National Center for Research Resources

Significant Items in House and Senate Appropriation Committee Reports

Biomedical Research Technology

The Senate in its report 102-104, p. 135, stated "The Committee is encouraged by efforts to expand the capability and use of existing high-performance computing resources for the extramural research community. Sufficient funds have been provided to continue this important initiative."

Action Taken or to be Taken: The FY 1992 appropriation for the NCRR includes $9,800,000 for high-performance computing and communications. The NCRR plans to fund two new centers in high-performance computing in FY 1992.

Biomedical Research Support

The Senate in its report 102-104, p. 136, stated "The Biomedical Research Support (BRS) Program consists of three components. The Biomedical Research Support Grant (BRSG) Program provides funds on a formula basis to institutions to support biomedical research needs not served by other programs. While no funds have been requested this year for the BRSG, the Committee has provided $15,000,000 to continue the BRSG program. The Committee urges the Director to use her contingency fund and transfer authority to further augment this program." The Senate stated further "The Committee recommends targeting more BRSG support to minority schools and other institutions that have less than demimimus (sic) amount in their research base. The Committee is supportive of the Department's ongoing effort to target those institutions that are still building a research infrastructure."

Action Taken or to be Taken: The FY 1992 appropriation for the NCRR includes $5,204,000 for the BRSG program. Although not specifically targeted, minority institutions, particularly those receiving funding through the Research Centers in Minority Institutions program, are eligible for BRSG awards.

Biological Models and Materials Research

The House in its report 102-121, p. 97, stated "The Committee expects that the biological models and materials research program will be maintained at least at the 1991 level and that new research project grants will be awarded."

Action Taken or to be Taken: The FY 1992 appropriation for the NCRR includes $8,327,000 for the Biological Models and Materials Research program, an increase of $269,000 over the FY 1991 level. Within this amount, the program expects to fund three new research project grants.

Research Centers in Minority Institutions

The House in its report 102-121, p. 97, stated "The Committee also strongly urges institutional (sic) cofunding of RCMI programs similar to the AIDS research that is being conducted."

Action Taken or to be Taken: The RCMI program of the NCRR is pursuing opportunities for Institute cofunding of research at RCMI institutions, particularly with the National Institute of Environmental Health Sciences, the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Dental Research, and the National Center for Human Genome Research.

NATIONAL INSTITUTES OF HEALTH

National Center for Research Resources

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1992 Amount Authorized	1992 Appropriation	1993 Amount Authorized	1993 Budget Request
Research and Investigation......	Section 301	42s241	Indefinite		Indefinite	
National Center for Research Resources......................	Section 479,480	42s287 287a,300a, and 5s332	Indefinite	$311,885,000	Indefinite	$327,565,000
National Research Service Awards	Section 487	42s288	Authorizing legislation is pending 1/	2,666,000	Authorizing legislation is pending 1/	2,666,000
Total Budget Authority.......				314,551,000		330,231,000

1/ This training authority is shared with other research training programs of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration.

NATIONAL INSTITUTES OF HEALTH

National Center for Research Resources

Appropriation History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1984	201,832,000	253,824,000 2/	230,031,000 2/	244,977,000 3/
1985	247,528,000	305,331,000 4/	305,298,000	304,025,000
1986	263,040,000	304,579,000 5/	305,739,000	305,667,000
1986 Sequester				-13,144,000
1987 6/	234,192,000	317,826,000	319,924,000	322,860,000
1988	280,415,000	346,652,000 7/	367,415,000	368,153,000
1989	319,977,000 8/	355,767,000 9/	367,987,000	358,608,000 10/
1990	263,313,000 11/	356,128,000	362,253,000	353,734,000 12/
1991	319,151,000	355,962,000	331,629,000	335,255,000 13/
1991 Sequester				-4,000
1992	320,975,000	309,200,000	317,227,000	314,551,000 14/
1993	330,231,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.

2/ Excludes $720,000 in NRSA training programs not considered.

3/ Includes $708,000 for NRSA training programs authorized under a Continuing Resolution.

4/ Excludes $775,000 in NRSA training programs not considered.

5/ Excludes $1,029,000 in NRSA training programs not considered.

6/ The budget estimate to Congress proposed that all funding for AIDS research be consolidated in the Office of the Assistant Secretary for Health. The House allowance consolidated all NIH AIDS funding in the Office of the Director, NIH; the Senate allowance and the appropriation spread funding among the institutes, including $6,142,000 for the Division of Research Resources.

7/ Does not include funding for AIDS research which was consolidated at the Secretary's level.

8/ The 1989 request excludes funds for AIDS research and education ($38,010,000) proposed for consolidation in the Office of the Assistant Secretary for Health.

9/ Excludes $2,220,000 in NRSA training programs not considered.

10/ Reflects a 1.2% reduction ($4,356,000) and a reduction of $23,000 as a result of improved procurement practices from the appropriated level of $362,987,000 as required by P.L. 100-436 Sections 517 and 215 respectively.

11/ The 1990 request excludes funds for the National HIV program ($44,643,000) proposed for consolidation in the Office of the Assistant Secretary for Health.

12/ Excludes enacted administrative reductions of $16,000 for procurement savings; $344,000 for extramural salary cap and $97,000 for salaries and expenses.

13/ Excludes enacted administrative reduction of $8,541,000.

14/ Includes enacted administration reduction of $669,000.

Justification

National Center for Research Resources

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
98	$335,806,000	97	$314,551,000	97	$330,231,000	---	+$15,680,000

General Statement

Biomedical research supported by the categorical components of the National Institutes of Health requires for its success the availability of the appropriate research resources. From the models required for research on diseases and disabilities, to the biomedical technology and instrumentation necessary to elucidate cellular and molecular structure, to the settings in which to conduct clinical research to understand diseases and develop new therapies, biomedical research must have access to the necessary resources in order to continue to expand and progress.

The National Center for Research Resources (NCRR) has the unique mission at the National Institutes of Health of providing resources to biomedical investigators across the spectrum of research activities supported by the NIH. This mission has several facets:

(1) The development of resources required to facilitate research at the cutting edge. The NCRR must anticipate future directions of research, so that appropriate resources will be in place when the research requires them.

(2) The support of shared resources for use by investigators today. These resources, are the locus of over 7,000 researchers, supported through well over $1 billion of categorical Institute funds, and include clinical research centers, primate research centers and biomedical research technology centers. Without these resources, the Institutes would need to provide the costly resources on a case-by-case basis, at increased cost.

(3) The provision of resources for research. The availability of appropriate models for human disease and the biotechnology and instrumentation necessary to further science knowledge is a cornerstone of the research enterprise, and essential to expanding the horizons of investigation.

(4) The enhancement of the research capability of the nation. This aspect of the NCRR mission is carried out through programs to increase the involvement of precollege students and their teachers in science, to develop the clinical and preclinical investigators of tomorrow, to develop and enhance the capacity of minority institutions to participate in the research enterprise, and to improve the condition of research animal facilities.

The mission of the NCRR is inextricably linked to the missions of the categorical Institutes of the NIH. The achievement of progress in the battle against disease and disability rests on innovation in research ideas, and is also reliant on the availability of the appropriate resources or tools with which to conduct the research.

Funding for the National Center for Research Resources during the last 5 years has been as follows:

	Amount	FTE
FY 1988	$347,377,000	89
FY 1989	340,898,000	89
FY 1990	337,105,000	90
FY 1991	335,806,000	98
FY 1992	314,551,000	97

Purpose and Method of Operation

The National Center for Research Resources provides the funding for the development, support and provision of research resources and for the enhancement of research capacity through its seven extramural programs, utilizing a variety of methods of institutional and investigator support. Research project grants and resource-related research grants provide support for innovative development of resources, including animal and other models and biotechnology. Resource centers constitute the largest proportion of the Center's budget, and provide support for networks of centers for conducting clinical research, for accessing the latest developments in biomedical research technology, and for carrying out research in the most appropriate models, whether primates, other mammals or nonmammalian models. The centers mechanism also supports the development of research capacity in minority institutions. Other research support includes provision of state-of-the-art instruments to be shared by several NIH-supported researchers, as well as biological materials for use by researchers. Other research support also includes the funding for improvement of animal facilities, career development, programs to encourage minority careers in science, and general research support. The research training program provides training for research veterinarians. The research contracts mechanism is used to support a variety of resources. The construction program provides for enhancement of the research facilities of minority institutions.

The Clinical Research Program supports the development and maintenance of specialized clinical research environments within large hospitals. The network of General Clinical Research Centers (GCRCs) provides clinical research facilities and staffing for over 4,600 inpatient and outpatient research studies carried out by more than 6,500 investigators who receive their primary research funding from other components of the NIH and PHS, other federal and state agencies, and the private sector. The GCRCs host an array of research that reflects the missions of all the NIH institutes and centers, including clinical studies in AIDS, cystic fibrosis, hypertension, and cancer.

The Biomedical Research Technology (BRT) Program provides access to advanced technologies used by the scientific community to solve complex problems of medical research. BRT centers support the development and application of technologies that are essential to biomedical research, but not widely available. Staff of the centers are gifted scientists who work closely with outside scientists, industry and other laboratories to develop new technological capabilities and apply them to emerging biomedical research problems.

The major objective of the Comparative Medicine Program (CMP), formerly known as the Laboratory Animal Sciences and Primate Research Program, is to support projects that focus on the most effective use of animals in research and the development of appropriate animal models. Support is provided for the Regional Primate Research Centers, a number of unusually valuable research animal colonies, and for essential animal facility improvement awards to help research institutions maintain compliance with PHS policies on animal welfare. The CMP also supports the only NIH extramural research training program which provides postdoctoral research training in laboratory animal science for veterinarians.

The Biomedical Research Support (BRS) Program provides additional resources to assist federally supported institutions in the conduct of biomedical research. The BRS formula grant program provides institutions with discretionary funds for pilot research projects, support of new investigators, bridge support, and other emergency research needs. Also within the BRS Program, the Shared Instrumentation Grant (SIG) program provides funds for the purchase of state-of-the-art research instruments to be shared by groups of PHS-grant supported biomedical researchers. The BRS Program also provides the support for the Minority High School Student Research Apprentice Program, a highly successful method for introducing minority students to the field of health research, as well as short term science laboratory opportunities to revitalize high school science teachers of minority students.

The Biological Models and Materials Research (BMMR) Program provides for the development and support of nonmammalian models for biomedical research, and provides critical biological materials to the research community. The BMMR Program is the focal point for the development of model systems such as lower vertebrates, invertebrates, cell and tissue culture systems, and nonbiological systems including mathematical and computer models, for biomedical research.

The Research Centers in Minority Institutions (RCMI) Program supports the development and enhancement of the research infrastructure of predominantly minority institutions that grant doctoral degrees in the health-related sciences, to enable these institutions to become more competitive in seeking NIH and PHS research project grant support.

The Research Facilities Improvement Program provides for the repair, renovation, modernization, and expansion of existing facilities for the conduct of research, specifically for Historically Black Colleges and Universities and other similar institutions. This program will enhance the capacity of these institutions to participate in the research enterprise through competitive awards to be partially matched by non-Federal funds.

The National Center for Research Resources also has an intramural component which provides a variety of resources to the intramural investigators associated with ICD programs on the NIH campus and in its vicinity. The intramural program is funded entirely through the Management

Fund and the Service and Supply Fund, charged back according to individual Institute usage. No funds have been requested through the appropriation for the intramural program.

Overall Budget Policy

The FY 1993 budget request for the National Center for Research Resources is $330,231,000, an increase of $15,680,000 over the FY 1992 level of $314,551,000.

In FY 1993, the NCRR will support 52 noncompeting research project grants (RPGs) and 27 new or competing RPGs in the Biological Models and Materials Research, Biomedical Research Technology and the Comparative Medicine Programs. The Small Business Innovative Research activity of the Center is also reflected in the RPG mechanism.

In FY 1993, the NCRR will support 201 research centers, in most cases at the same level as in FY 1992. The NCRR will maintain support to 74 general clinical research centers, 7 regional primate research centers, 34 laboratory animal sciences centers, 6 biological models and materials research centers, and 17 research centers in minority institutions at the same level of funding as FY 1992. The request includes $3,000,000 to continue to address repair and renovation needs of the regional primate research centers. The NCRR will also support 63 biomedical research technology centers, with an increase of approximately 2.2 percent provided for support of an additional center in high performance computing and communications.

All activities in the "Other Research" category will be continued at the FY 1992 level. The NCRR will fund approximately 104 Biomedical Research Support Grant (BRSG) formula awards, at a level of $5,204,000. Approximately 36 awards will be made in the Shared Instrumentation Grant program for $8,758,000. The Minority High School Student Research Apprentice Program will be funded at a level of $8,900,000, permitting the support of approximately 3,600 high school students and 475 science teachers in this enrichment program. Approximately 11 research career awards and 46 animal facilities improvement grants will be made, and there will be approximately 42 awards in the other research-related category.

The FY 1993 request for research training is $2,666,000, the same level as in FY 1992. The Center plans to support approximately 76 institutional full-time training positions, and 6 individual fellowships.

The budget request for research and development contracts is $3,350,000, the same level as in FY 1992. This level will enable the Center to support seven contracts in FY 1993.

The FY 1993 budget request for Research Management and Support is $14,307,000, an increase of $668,000 or 4.9% over the FY 1992 level. This increase will cover built-in administrative cost increases. Approximately 97 FTEs will be supported, the same level as in FY 1992.

National Center for Research Resources

Clinical Research

Authorizing Legislation - Sections 301, 479, 480, and 487 of the Public Health Service Act. 1993 Authorization: Indefinite.

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$118,444,000	$126,882,000	$126,882,000	---

The General Clinical Research Centers (GCRC) Program supports a national network of clinical research facilities, distributed within 30 states, along with professional staffing for more than 4,600 inpatient and outpatient clinical research studies. In partnership with the other National Institutes of Health categorical Institutes and Centers as well as with other Federal agencies and research funding sources in the private sector, the GCRCs support the clinical research of more than 6,500 investigators. The research carried out across the network of GCRCs can be subdivided into four broad areas: clinical trials, biotechnology, prevention and other research, which includes studies of physiologic mechanisms and the pathophysiology of diseases. The configuration and access to the GCRCs provide ready translation of basic research and novel biotechnologies as clinical research tools to define the underlying causes and more effective treatment of an array of diseases and disorders of both adults and children, reflecting the leading edge of biomedical research in several areas, including molecular medicine, nutrition, aging, reproduction, cancer, diabetes, acquired immunodeficiency syndrome (AIDS) and maternal and child health. The GCRC Program works closely with the other components of the National Institutes of Health to form a partnership which provides a cost effective approach to carrying out high quality clinical research for the improvement of the Nation's health and the quality of life of its citizens.

Funding for the Clinical Research Program during the last 5 years has been as follows:

	Amount
FY 1988	$102,601,000
FY 1989	108,730,000
FY 1990	115,960,000
FY 1991	118,444,000
FY 1992	126,882,000

Rationale for the Budget Request

The FY 1993 budget request for the Clinical Research budget activity is $126,882,000, the same as the FY 1992 estimate.

Alzheimer's Disease

Investigators have found a gene for amyloid precursor protein in two recent generations of a family with familial, early onset Alzheimer's disease. Analysis of DNA from living and deceased family members revealed a specific mutation believed to be located in a DNA region that codes for amyloid protein. Direct sequencing of DNA from a family member with Alzheimer's led to the identification of a single amino acid substitution in the relevant area of the amyloid precursor protein. The mutation correlated with the presence of Alzheimer's disease in all patients studied and was absent in Alzheimer's-free family members and 100 unrelated individuals. This study suggests that the mutation may be the inherited factor causing dementia in individuals with this form of Alzheimer's disease.

Atherosclerosis

The treatment of postmenopausal women with estrogens lowers the concentration in the blood of low-density lipoprotein (LDL) -- the so-called "bad" lipoprotein -- and increases the level of high-density lipoprotein (HDL) -- the "good" lipoprotein -- and may also reduce the risk of cardiovascular disease. In recent years the doses of estrogen prescribed for postmenopausal women have been lowered to those levels that prevent osteoporosis and relieve menopausal symptoms. To ascertain whether those lowered doses of estrogens favorably affect lipids, a study was undertaken which confirmed that oral estrogens, taken daily at the lowered dose levels, reduced LDL concentrations and increased HDL levels which may protect women against atherosclerosis.

Osteoporosis

In a recent study investigators found that the bone density of both the radius (one of the bones of the forearm) and the spine of black women is approximately 6.5 percent higher than that of white women of similar age, weight, and socioeconomic background. Since the difference in bone density found in the two groups could not be attributed to socioeconomic class, smoking, dietary calcium intake, vitamin or mineral supplementation, exercise levels, or use of prescription drugs, it appears to represent a genetic difference between the races. Moreover, the results showed that white women lose bone mass both before and after menopause, while black women build up bone mass before menopause and lose it at a lower rate after menopause than do white women. The research team is now conducting a longitudinal study of bone metabolism in white and black women. The capacity to predict who is at risk for fractures -- and an understanding of why osteoporosis develops and how it can be prevented -- will have an important economic and health impact for postmenopausal women.

Colon Cancer

Both genetic and environmental factors are involved in the development of colorectal cancer. There is a growing evidence that colon cancers arise from polyps and that removal of the premalignant lesion, the adenomatous polyp, prevents cancer occurrence. Scientist have established that the vast majority of colonic adenomatous polyps, and therefore colorectal cancers, occur in individuals with an inherited susceptibility. DNA was obtained from many of the individuals and the polyp susceptibility gene was mapped to chromosome 5.

The capacity to identify carriers of this gene should lead to targeting of that portion of the population most likely to benefit from endoscopy screening.

Nitrogen Metabolism

A test developed by researchers at a General Clinical Research Center may help physicians identify women with a rare genetic defect that impairs the body's ability to metabolize nitrogen compounds. Treatment can prevent the metabolic crises that occur in some of these women when their blood ammonia concentration rises to life-threatening levels. The disorder results from a defective gene on the X chromosome. The gene codes for an enzyme involved in production of urea, a compound produced by the liver and excreted with the urine as a nitrogen waste product. Incomplete production of urea due to a defective enzyme can cause episodes of hyperammonemia, in which ammonia accumulates in the blood, leading to lethargy, vomiting, coma, swelling of the brain, and even death in severe cases. Like many other genetic disorders, this deficiency was first recognized in severely affected infants. Recently the potentially serious effects of this deficiency in adult women was recognized. It is not known what triggers hyperammonemia in women who carry the defect, nor is it clear why the risk of ammonia intoxication is particularly high after giving birth. The researchers have now developed a convenient, reliable and inexpensive test to identify women carrying the defect.

Aquired Immunodeficiency Syndrome (AIDS)

In FY 1991, 59 GCRCs supported 22 percent more AIDS-related research projects than in the previous fiscal year. Phase 1 and 2 clinical trials are the primary focus of those studies for both HIV-infected children and adults. Many of the studies have progressed from phase I clinical evaluations to phases II and III; some have moved from the carefully controlled conditions of the GCRCs to wider clinical testing at many medical centers throughout the United States. In a multicenter, double-blind, controlled study children treated with intravenous immunoglobulin (IVIG) had significantly fewer serious bacterial infections than did pediatric AIDS patients treated with a placebo. The study, which started in March 1988, enrolled 372 symptomatic HIV-infected children at 28 centers; because of benefits seen in the IVIG-treated children, the study was terminated in January 1991.

Breast Cancer

Scientists reported that proliferative breast disease (PBD), a significant risk factor for the development of breast cancer, is an inherited trait in families that have a high prevalence of either premenopausal or postmenopausal breast cancers. The investigators studied 20 extended families in which at least two first-degree relatives (such as mother, sister, or daughter) had breast cancer. Women who were not genetically related but were spouses of male members of the families participated as control subjects. Analysis of tissue aspirated from the breasts of all women in the study revealed proliferative breast disease in 35 percent of the clinically normal first-degree relatives of the women who had breast cancer but in only 13 percent of the control women, providing evidence of a gene for proliferative breast disease.

Diabetes

A team of scientists reported that the excessive accumulation of glucose-modified proteins and peptides, called advanced glycosylation endproducts (AGEs), appears to be involved in the chronic complications of diabetes. The scientists measured circulating and tissue AGE levels in diabetic and nondiabetic patients who had varying degrees of kidney failure. They found the AGE content of specimens taken from the arterial walls of diabetic patients with endstage kidney disease to be almost twice as high as those from diabetic patients without kidney disease. All of the diabetic patients' arterial wall specimens had significantly higher levels of AGEs than did the specimens from nondiabetic normal controls. The concentration of AGE-peptides circulating in the blood of diabetic patients correlated with the severity of their kidney dysfunction.

Gene Therapy

The introduction of genes into human somatic cells and adequate expression of the inserted gene to correct or replace defective genes is now possible for some genetic diseases. This is the ultimate in biotechnology transfer -- bench research interfacing with the bedside. In early 1992, investigators at a General Clinical Research Center will begin the first gene therapy for patients with a lethal hereditary illness, familial hypercholesterolemia - a rare disorder which results in excess cholesterol buildup in tissues and leads to early heart attacks. New genes will be inserted into liver cells of affected patients so that liver cells can make the receptor protein necessary for removing cholesterol from the blood. This approach may eventually be used for treating other genetic liver disorders, including phenylketonemia, hyperbilirubinemia, and urea cycle defects which impair the liver's capacity to remove waste products from the blood.

Gene therapy is embryonic but is developing rapidly so that gene therapy for several of the 5,000 diseases which result from a single gene defect is now possible or will be possible in the near future. In addition, modified forms of gene therapy have been used to develop novel therapies for cancer. This area will be expanded considerably over the next few years.

National Center for Research Resources

Biomedical Research Technology

Authorizing Legislation - Sections 301, 479, 480, and 487 of the Public Health Service Act. 1993 Authorization: Indefinite.

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$40,882,000	$46,320,000	$48,885,000	+$2,565,000

The purpose of the Biomedical Research Technology Program is to provide the scientific community access to advanced technologies needed to solve the problems of biomedical research. This purpose is accomplished by funding centers for development and application of technologies that are essential to biomedical research, but not widely available. These centers are staffed by scientists and engineers who work closely with outside biomedical scientists, industry, and other laboratories to both develop and apply new technological capabilities to biomedical research problems. Research project grants and small grants support future-directed activities -- new instrument and technology development and new research ideas.

Funding for the Biomedical Research Technology Program during the last 5 years has been as follows:

	Amount
FY 1988	$41,734,000
FY 1989	40,943,000
FY 1990	39,715,000
FY 1991	40,882,000
FY 1992	46,320,000

Rationale for the Budget Request

The FY 1993 budget request for the Biomedical Research Technology budget activity is $48,885,000, an increase of $2,565,000 or 5.5 percent over the FY 1992 estimate of $46,320,000.

Technology development over the past several years has changed the nature of basic biomedical research. Fundamental biological processes like the immune response and genetic transformations that lead to cancer can now be studied directly in some cases, truly a major step towards reaping the benefits of years of basic science research support by the National Institutes of Health. Nowhere has this been more evident than in the explosive growth in structural biology studies of proteins, viruses, and nucleic acids. The Biomedical Research Technology Program has contributed directly to this growth by providing biomedical scientists with access to necessary technologies such as synchrotron x-ray sources, high-performance computing centers, instrument-based centers, and image-analysis centers. The following are illustrations of recent research accomplishments at these resource centers.

Acquired Immunodeficiency Syndrome (AIDS)

The human immunodeficiency virus that causes AIDS includes a protease enzyme that is required for infectivity. A group of scientists determined the structure of this enzyme and of an enzyme-inhibitor complex in an effort to find specific treatments for AIDS that involve inactivating this enzyme. Some success in this effort has been reported by a group using a structure-based computer-assisted method to search a molecular structure database for drugs that could fit in the pocket of the dimeric enzyme. The search suggested that a known antipsychotic agent, haloperidol, would be a good candidate. Haloperidol itself is toxic at the high doses that would be required to inhibit the AIDS virus, but it may be a useful lead compound for the development of a new, antiviral pharmaceutical.

Protein Crystallography

In 1991, the first report on the three-dimensional molecular structure of a protein kinase enzyme appeared. The crystal structure of the catalytic subunit of the cyclic AMP-dependent kinase involved 6 years of effort in its elucidation. Protein kinases are an important family of enzymes that play key roles in many of the pathways by which hormones, growth factors, neurotransmitters, and toxins have their effects. Research into the way these enzymes function has been hampered by lack of information about the actual structure of a protein kinase; this structure thus represents a significant advance in understanding biochemical events related to a variety of diseases.

Mass Spectrometry in Cancer Research

Mass spectrometry facilities provide investigators in biology, chemistry, and medicine access to the specialized equipment and techniques of mass spectrometry for those research problems that require it. Some recent research includes the detection and characterization of inborn errors of fatty acid oxidation in children born with carnitine deficiency - a life-threatening condition. In another research study, a variety of gangliosides, special types of glycolipids found on the cell membrane, shed by tumor cells has been characterized by mass spectrometry, and scientists are investigating the possibility that gangliosides may promote tumor growth by suppressing the immune response. This represents a new approach to the study of human tumors and leukemias, since leukemia cells behave in a similar fashion.

Laser Treatment for Atherosclerosis

Scientists have developed a prototype laser system for removing atherosclerotic plaque from diseased arteries. The idea of using catheter-delivered laser light to cut away diseased tissue, leaving the normal tissue intact, has been around for many years but, until this prototype was developed, previous approaches failed because the laser easily damaged normal arterial tissue, even to the extent of perforating the arterial wall. The prototype system uses 12 optical fibers arranged around the circumference of the catheter to deliver laser light to the tip. A weak laser pulse is first sent down each fiber to spectroscopically analyze the tissue for the presence or absence of atherosclerotic plaque in contact with the tip. If plaque is detected at the end of any three or more adjacent fibers, a very brief but intense laser pulse is delivered down those same fibers to vaporize a shallow layer of plaque. The cycle of spectroscopy, analysis, and cutting as necessary is repeated as the catheter advances through the diseased artery. This prototype system is now being tested in clinical trials.

Elucidation of Biomedical Structures

The emergence of computer graphics that give the user the impression of being in the computer-generated picture - referred to as virtual reality - provides new opportunities for research on biomolecular structures. For example, a group of researchers has developed a molecular docking system that involves use of a remote manipulator to fit small molecules or drugs into binding sites on the enzyme dihydrofolate reductase. The system provides force feedback to the user reflecting good or bad fits, and controlled tests have indicated that biochemists found the system extremely rapid and useful. This is an example of a new technology being adapted and developed for broad use.

Synchrotron Facilities

During FY 1992, the Biomedical Research Technology Program plans to expand support levels in the areas of synchrotron facilities and high-performance computing. The Department of Energy is currently constructing two major new synchrotron facilities to serve scientists in the United States. The biomedical research community has intensively used the three existing U.S. synchrotron facilities supported by the NCRR; many scientists have traveled to Europe or Japan for access to such facilities because of the limited time available within the U.S. The NCRR expects to fund one or more access ports at the new synchrotron centers for use by the NIH-supported research community.

High Performance Computing

The Biomedical Research Technology Program is in the process of incorporating two new high-performance computing centers into its resource center program. Both of these activities will feature the development of innovative algorithms and software for use on state-of-the-art parallel processing architectures. One of these resource centers will focus on theoretical simulation of biological systems with multi-disciplinary effort receiving strong input from expertise in quantum chemistry, statistical mechanics, molecular modeling, and biophysical theory. The other resource center will develop efficient portable parallel programs for determining molecular structure and supporting other biomedical modeling activities. These resource centers will provide necessary technological support for the basic research related to immunobiology, virology, and a number of other areas of structural biology. An additional center is planned for FY 1993.

National Center for Research Resources

Comparative Medicine Program

Authorizing Legislation - Sections 301, 479, 480, and 487 of the Public Health Service Act. 1993 Authorization: Indefinite.

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$68,481,000	$72,947,000	$73,244,000	+$297,000

The Comparative Medicine Program (CMP) of the National Center for Research Resources (NCRR) helps meet the needs of the biomedical and health research community in the area of laboratory animal science and nonhuman primate resources. CMP activities are multidisciplinary in scope and address needs that extend beyond the categorical interests of a single NIH Institute. The Comparative Medicine Program supports research, animal resources, and training through grants, cooperative agreements, and contracts. The Regional Primate Research Centers Program, utilizing grants, supports a national network of seven centers for primate research. The AIDS Animal Models Program supports resources and research that identify, develop and make available animal models for AIDS-related research through cooperative agreements and grants.

Funding for the Comparative Medicine Program (formerly the Laboratory Animal Sciences and Primate Research Program) during the last 5 years has been as follows:

	Amount
FY 1988	$63,441,000
FY 1989	66,887,000
FY 1990	67,696,000
FY 1991	68,481,000
FY 1992	72,947,000

Rationale for the Budget Request

The FY 1993 budget request for the Comparative Medicine budget activity is $73,244,000, an increase of 0.4 percent over the FY 1992 estimate of $72,947,000.

Laboratory Animal Sciences Program

The Laboratory Animal Sciences Program (LASP) helps to improve the health and quality of laboratory animals, determine environmental and welfare requirements of these animals, and establish and maintain special animal colonies for research. The program also awards grants to develop, characterize, and improve animal models of human disease; to diagnose, study, and control diseases of laboratory animals; and to develop and improve institutional animal research and resource programs. The LASP continues to support projects to improve and maintain extramural institutional animal facilities consistent with Federal regulations and PHS Animal Welfare Policy. Awards are made for postdoctoral research training for veterinarians in laboratory animal medicine and comparative pathology. Special Emphasis Research Career Awards (SERCAs) provide support for additional veterinarians to receive advanced research training needed to become independent investigators.

The LASP awards grants for both basic and applied (or resource related) research in laboratory animal science. These diverse activities continue to yield information helpful for improving the quality, health, and well-being of research animals, developing more appropriate animal models for research, and impacting favorably on the efficiency and numbers of animals used in research. For example, such research has been central to recognizing and dealing with Mouse Hepatitis Virus, an infection causing immunologic damage which has frequently confounded studies dependent on the species most widely used in research. Research on cryopreservation technology has made possible the banking of mouse germplasm (eggs and embryos) and reductions of the numbers, and cost, of mice that must be maintained by conventional breeding. In the animal model development arena, gene therapy studies in mice showed real promise for dealing with serious inherited children's diseases such as severe combined immunodeficiency.

Support for laboratory animal resources has always constituted a major activity in the LASP. Included in this category are grants for laboratory animal diagnostic and investigative laboratories, support for maintenance of animal models and special colonies, for nonhuman primate resources, and for information and reference centers. Beginning in FY 1992, support for diagnostic and investigative laboratories will be phased out. Replacing them will be awards for Comparative Medicine Research program projects. This change represents an effort to stimulate interest in and to use resources more effectively for exploiting the many research opportunities that exist in this area.

Regional Primate Research Centers Program

The Regional Primate Research Centers (RPRC) Program provides specialized facilities for nonhuman primate research, experienced personnel, and appropriate research environments to support the development of nonhuman primate models and provide these research resources for studies of critical importance to understanding human health problems and disease processes. Nonhuman primates are important to biomedical research because they share about 90% of the human genome and exhibit many biological characteristics that are identical or very similar to humans.

Some 1,200 U.S. scientists whose research is supported by the National Institutes of Health and other governmental and private organizations use these centers. In addition to serving investigators on site, the centers distribute more than 10,000 specimens per year to other U.S. laboratories. These centers are the focal points for the development and study of nonhuman primate models for research on cancer, cardiovascular diseases, Alzheimer's disease, AIDS, leprosy and Parkinson's disease, as well as other diseases and conditions common to man. The following are recent accomplishments at the RPRCs.

Glaucoma

Scientists have found that the ciliary muscle in aging rhesus monkeys loses its ability to contract, probably due to a loss of elasticity of the tissues tethering the muscle to the back of the eye. As a result, the eyes of aging rhesus, as in humans, lose their ability to "accommodate" (focus on objects close to the face) and to discharge fluid. These findings have significant implications for the pathophysiology and therapy of human presbyopia and glaucoma. For example, because focusing and fluid drainage are both linked to the ciliary muscle, stimulating the muscle with drugs to contract (an important treatment for glaucoma) can also blur vision by causing the eye to over-focus. The researchers are now testing procedures to separate these two functions of the ciliary muscle in an effort to design more selective drugs to treat glaucoma without the unwanted effects on focusing.

Acquired Immunodeficiency Syndrome (AIDS)

Monkey AIDS virus - simian immunodeficiency virus (SIV) - is very similar to the viruses that cause human immunodeficiency virus (HIV) diseases. An SIV of precise and known genetic structure was administered to two pigtailed macaques. Viral gene sequences from the animals were analyzed at regular intervals following inoculation, and the precise genetic structure of the part of the virus that determines the coat structure was defined. Whereas five regions of genetic material had been known to show considerable variation in strains of the virus taken from different individuals with AIDS, only two were found in this study to vary over time in a particular individual. Furthermore, as the structure of the virus evolved, it tended toward the same new structure in both animals as they developed full-blown AIDS. This observation suggests that, while viruses with a wide range of coat forms may be capable of infecting the individual, only one or a few forms may be capable of escaping the immune system's control.

These findings suggest potential strategies for developing vaccines directed at those portions of the coat which do not undergo rapid change. A vaccine directed at the form of virus which escapes immune control might prevent infection from progressing to fatal AIDS disease. The findings may also advance attempts to identify the specific protective immune process that the virus evolves to elude.

AIDS Animal Models Program

The AIDS Animal Models Program promotes the characterization and validation of existing models and coordinates these efforts with other NIH Institutes. Support of breeding projects is a major part of this program, particularly the National Chimpanzee Breeding Program and projects that are providing specific-pathogen-free (SPF) rhesus monkeys for AIDS investigators.

Chimpanzee Breeding and Research

The Chimpanzee Breeding and Research Program (CBRP) is the first and only national program to converge the expertise and experience of chimpanzee breeders and researchers for an allied effort. This program is designed to provide a stable supply of healthy chimpanzees for biomedical research and to perpetuate the captive chimpanzee population in the United States. Offspring from the CBRP are available for Public Health Service-sponsored behavioral studies and biomedical research, including studies on AIDS.

The CBRP companion research studies complement and advance the ultimate goals of the program. Studies on genealogy have produced data that show a large fraction of the genetic variation is present in the captive chimpanzee population and that through controlled breeding techniques, the risk of inbreeding has been minimal. Studies are underway to identify behavioral and developmental factors that accurately predict the chimpanzee's socio-sexual behavior. Studies of reproductive physiology provide insights into the causes of lowered human fertility.

Specific Pathogen Free (SPF) Rhesus Breeding

Characterization and demographic status of the SPF colonies have been achieved and it is now possible to estimate the production rate over the next 5-6 years. The combined SPF colonies currently total over 1,300 animals with 560 breeding females and will produce over 200 SPF yearlings in 1994. Most of the colony's young males and retired breeders are currently available for AIDS research, with priority given to projects sponsored by the Public Health Service.

Companion research activities in virology, genetics and behavioral enrichment play a major role in support of program goals. Virology reference laboratories have performed over 8,000 tests to insure the SPF status of the colony animals. Research projects currently underway include the assessment of evolutionary concepts of herpes viruses by biochemical, immunological, and molecular biological approaches; development of recombinant reagents for diagnostic research; identification of effective antiviral strategies and design of putative vaccines; and elucidation of host-virus interactions during pathogenesis.

Impact Data

	FY 1991	FY 1992	FY 1993
Laboratory Animal Sciences................	$26,320,000	$26,585,000	$26,143,000
Regional Primate Research Centers.................	36,819,000	40,574,000	40,574,000
AIDS Animal Models........	5,342,000	5,788,000	6,527,000
Total..................	68,481,000	72,947,000	73,244,000

National Center for Research Resources

Biomedical Research Support

Authorizing Legislation - Sections 301, 479, 480, and 487 of the Public Health Service Act. 1993 Authorization: Indefinite.

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$64,458,000	$22,862,000	$22,862,000	---

The Biomedical Research Support Program (BRSP) encompasses three grant programs that help PHS-funded biomedical institutions meet critical research needs. These programs, which promote innovation, bolster research infrastructure, and strengthen science education at the precollege level, are the Biomedical Research Support Grant (BRSG) Program, the Shared Instrumentation Grant (SIG) Program, and the Minority High School Student Research Apprentice (MHSSRA) Program. In FY 1991 the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) and NIH developed the Science Education Partnership Award (SEPA) Program, which aims to increase the science literacy both of students in grades kindergarten through 12 and of the general public. The NIH component of the program is administered by BRSP.

Funding for the Biomedical Research Support Program during the last 5 years has been as follows:

	Amount
FY 1988	$90,918,000
FY 1989	88,762,000
FY 1990	78,838,000
FY 1991	64,458,000
FY 1992	22,862,000

Rationale for the Budget Request

The FY 1993 budget request for the Biomedical Research Support budget activity is $22,862,000, the same as the FY 1992 estimate.

Biomedical Research Support Grant (BRSG)

The BRSG Program complements and enhances the support of biomedical and behavioral research conducted through research project grants. It provides funds for small-scale, short-term support of research projects, using mechanisms that allow rapid response to unanticipated needs and new opportunities. It responds to the need for preliminary explorations of new ideas and techniques, and for flexible funding that can allow an investigator to exploit new opportunities that could not be anticipated in previous budgets. In FY 1992 the BRSG program will be changed significantly to increase the impact of the awards: awards will be $50,000, made competitively, and distributed equally among the top third, the middle third and the lower third of eligible institutions.

Bone Growth in Rats

A BRSG-funded pilot study recently showed that negatively charged microscopic beads of Sephadex, a starch-like material, stimulated bone growth in rats when implanted in bony defects of the jaw and cranium and when applied to the rats' nasal bone surface. The investigators found that new bone forms only if negatively charged beads establish contact with existing bone or are placed inside a bony environment. The scientists believe that growth factors may be attracted by the charged particles.

Although clinical devices generating electrical fields are available to treat bony nonunions, these devices are too bulky to be practical in the craniofacial skeleton. It is not yet clear how effective negatively charged beads or other negatively charged implants might be in clinical applications, but the scientists suggest that further investigations are warranted, especially when directed at possible periodontal and orthopedic applications for the nation's aging population.

Shared Instrumentation Grant (SIG) Program

Expensive, high technology instrumentation is a prerequisite for biomedical research. By providing sophisticated, complex instruments the SIG Program allows groups of NIH grantees to enhance the goals of their ongoing research programs. Rapid technological advances have opened new scientific areas and increased the rate at which research data can be obtained; the sensitivity of new analytical techniques and tools allow more powerful research. Examples of these new instruments include, but are not limited to, powerful new NMR imagers, coupled hybrid mass spectrometers, scanning laser confocal microscopes, and gene sequencing equipment.

To achieve significant research advances in a highly competitive, technologically oriented research environment, researchers require access to the unique capabilities provided by currently available elaborate instrumentation. The SIG Program offers a cost-effective method for groups of NIH grantees (an average of eight users) to compete for an instrument in the $100,000 to $400,000 cost range on the basis of their need and the instrument's ability to enhance and extend the research goals of their ongoing NIH-funded projects. Some recent advances made possible through the use of equipment purchased with SIG awards follow.

Kidney Function Probed With Interactive Laser Cytometry

An abnormal urinary albumin level provides a sensitive marker of the onset of kidney disease. A better understanding of the mechanism of albuminuria, or albumin loss into the urine, may be a key to preventing and treating kidney disease. For many years albuminuria has been attributed to altered permeability of the basement membrane that lines the glomeruli of the kidney. New light is being focused on the problem with the aid of an interactive laser cytometer awarded to 13 NIH-funded researchers. This relatively new instrument analyzes, selects, and sorts anchored cells, permitting single and multiple serial measurements on selected individual cells. Two-and-three dimensional confocal imaging can also be carried out. Now through the use of all the features of the interactive laser cell cytometer awarded by the SIG Program and using a novel technique to isolate glomerular basement membranes, the NIH supported investigators have reported that glomerular cells themselves, not the basement membranes, are the major determinant of permeability.

Graft-Versus-Host Disease

Using special imaging and cell sorting instrumentation, several NIH grantees have identified a novel T-cell in the target organs of mice that developed graft-versus-host (GVH) disease after transplantation of foreign bone marrow. GVH disease is a serious and potentially fatal complication of organ transplantation between incompletely matched individuals. The scientists made their discovery using an interactive laser cytometer and other accessories purchased through a SIG award.

The investigators point out that cells having the same characteristics as the newly identified T-cell are the predominant lymphocytes in the epidermis, or outer layer of skin. These cells have also been detected in the spleens of mice with GVH disease three weeks after transplantation but are not found in transplanted mice without GVH disease. The scientists found that the cells could cause the epidermal damage characteristic of GVH disease when transferred into other mice; the cells are therefore considered effector cells of cutaneous GVH disease.

Environmental Toxins and DNA

NIH funded researchers have found a powerful 500 Mhz Nuclear Magnetic Resonance (NMR) spectrometer system purchased through a SIG award to be essential for learning how toxic chemicals damage mammalian DNA and initiate cancers, birth defects, and other abnormalities at the molecular level. The NMR interfaced to a computer graphics workstation has permitted newer and faster one-dimensional and two-dimensional data acquisition and processing capabilities not previously available, allowing molecular models to be graphically visualized in various plans and under different conditions.

Much of the research has centered on studying modifications of DNA by benzo[a]pyrene, a cancer causing component of tobacco smoke, and by the industrial chemical styrene. The latter chemical is believed to pose a threat to the chemical industry workers who produce it. DNA interactions with aflatoxin, a toxic compound formed by mold that contaminates foodstuffs such as corn and peanuts, is also being examined with the aid of the NMR spectrometer.

Minority High School Student Research Apprentice (MHSSRA) Program

A key objective of the MHSSRA Program is to interest minority students in pursuing careers in health-related research and in health care. Demographic patterns indicate that such minority representation is becoming more and more urgent in the health-care professions, including both researchers and practitioners.

The MHSSRA Program motivates and stimulates interest in biomedicine by providing high school students with up to 8 weeks of hands-on experience in basic or clinical laboratories. The students learn the underlying concepts of molecular and cell biology, evolution, development and reproduction, heredity, and ecology by carrying out actual laboratory experiments as part of a scientific investigation. In this way the students' curiosity and understanding of scientific concepts reach far beyond that achievable through the ordinary classroom and textbook experience.

In FY 1991 the MHSSRA Program was extended to include a high school science teacher component. To qualify, a science teacher must be a member of a minority group or teach a significant number of minority students. The program is designed to provide high school science teachers with an in-depth laboratory experience in biomedical sciences during a summer internship at a local university, health professional school, or research organization, offering these science teachers the opportunity to update their skills, learn modern research techniques, and broaden their knowledge of fundamental principles of biomedical sciences - an opportunity that can translate into a lively enthusiasm for science education in the classroom. Some examples of the successes of this program follow.

A science teacher assisted in clinical research for 8 weeks during the summer of 1991. With an immunologist as his mentor, the teacher coupled his computer skills with audiovisual techniques in research to develop visual methods of detecting early signs of rejection in heart transplant patients and in laboratory animals.

During FY 1991 a student in the MHSSRA Program was one of 40 finalists in the country's most prestigious precollege science competition, the 50 year old Westinghouse Science Talent Search (WSTS). The 17 year old high school senior had been selected in 1990 to serve as an apprentice in the MHSSRA Program at a plant pathology laboratory. She devoted her apprenticeship primarily to a project on the genetic engineering of pest resistant poplar trees; in this context she helped develop a time saving test to assess whether genes conferring pest resistance were transferred from potatoes to poplars. She attributed her 1991 selection by the WSTS partly to her research paper on the electrical propagation of proteinase inhibitor II in poplar hybrids.

Science Education Partnership Award (SEPA)

The Department of Health and Human Services has long been concerned with U.S. science literacy, which also has a profound impact on the Alcohol, Drug Abuse, and Mental Health Administration and NIH and their capacity to carry out their mission. U.S. public, social, and economic health depends increasingly on the population's understanding and use of science and technology.

The objective of the FY 1991 SEPA program administered by the BRS Program for NIH is to increase the science literacy of students in kindergarten through grade 12 as well as the general lay public. NIH awards were made for the development of model programs that span the range of science education, including a national video education program; a traveling AIDS museum exhibit; simple hands-on laboratory experiments for elementary and middle school students; biotechnology research experiences for students and teachers; and health-promoting outreach programs for inner city and rural communities. If successful, these innovative pilot programs will be replicated across the country to increase the number of citizens knowledgeable about science.

Impact Data

	FY 1991	FY 1992	FY 1993
Biomedical Research Support Grants (BRSG)...	$22,250,000	$5,204,000	$5,204,000
Shared Instrumentation Grants..................	32,658,000	8,758,000	8,758,000
Minority High School Student Research Apprentice Program......	8,235,000	8,900,000	8,900,000
Science Education Partnership Award (SEPA).......	1,315,000	---	---
Total..................	64,458,000	22,862,000	22,862,000

National Center for Research Resources

Biological Models and Materials Research

Authorizing Legislation - Sections 301, 479, 480, and 487 of the Public Health Service Act. 1993 Authorization: Indefinite.

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$8,058,000	$8,327,000	$8,477,000	+$150,000

The Biological Models and Materials Research Program (BMMRP) has a dual mission: the development and support of nonmammalian model systems, such as invertebrates, lower vertebrates, cell and tissue culture systems and nonbiological systems, including mathematical and computer models for biomedical research into human disease; and the support of resource facilities that provide critical biological materials for the biomedical research community. These programmatic activities are supported through investigator-initiated grants, cooperative agreements, resource center grants, resource-related grants and contracts.

Funding for the Biological Models and Materials Research Program during the last 5 years has been as follows:

	Amount
FY 1988	$2,593,000
FY 1989	3,727,000
FY 1990	5,345,000
FY 1991	8,058,000
FY 1992	8,327,000

Rationale for the Budget Request

The FY 1993 budget request for the Biological Models and Materials Research budget activity is $8,477,000, an increase of 1.8 percent over the FY 1992 estimate of $8,327,000.

High Connectivity Models

To advance its objectives during FY 1991, the BMMRP solicited proposals from the research community to encourage the development of "high connectivity" models. These are organisms or biological systems where a large body of knowledge is available and extensive cross information or connection with other systems has resulted. Organisms are also connected or crosslinked by their sharing of functions and properties with other organisms across many taxa. The information obtained from this type of research can be integrated and transferred from one taxon to another with the eventual goal of broadening understanding of the normal and pathological states of man. Some of the research project grants that were awarded by BMMRP are summarized here to indicate the great diversity of model systems that can be employed in biomedical research. In FY 1991, the BMMRP funded studies that include: the use of a reptilian model to understand the regulation of apoliprotein metabolism; the development of mathematical and computer models to test theories of the immune system; the use of yeast to study steroid hormone action; the isolation and characterization of the Major Histocompatibility Complex genes from frogs to expand our knowledge about the evolution of immunity; experimentation with fruit flies to understand how growth factors contribute to embryonic development; the development of a supercomputer mathematical model of the mammalian kidney to understand both normal and diseased function; and the use of cultured mammalian cell lines to understand how oxygen free radicals damage DNA and contribute to a number of human pathological conditions.

Marine Models

BMMRP recognizes that the great biodiversity of nonmammalian marine organisms is virtually untapped in biomedical research. The development of sophisticated technologies can easily be adapted to these organisms which will provide new understanding of biological processes. Consistent with its mission to develop nonmammalian models and in light of the emerging importance of marine biotechnology, the BMMRP cosponsored a 3 day international conference on marine biotechnology attended by over 400 researchers; funded a resource-related grant to reduce the cost of production and increase the availability of cephalopods (octopus, squid and cuttlefish) for research; and awarded research project grants on the development of transgenic aquatic organisms, including fish and sea urchins. The advent of transgenic technology, the ability to introduce foreign genes into a developing embryo, not only will produce interesting and useful models of human genetic disorders, but also constitutes a powerful approach to examine gene regulation, development and pathogenesis.

Biomaterials

As part of the BMMRP's mission to provide critical biomaterials to the research community, the Program supports a number of resource facilities that assist individual scientists by providing biomaterials and organisms; maintaining normal and abnormal cells of many species; establishing methods of laboratory culture of nonmammalian marine organisms, including sea snails, octopus, and squid; acquiring and distributing microorganisms, including viruses, bacteria, fungi and yeast; and developing collections of valuable biomaterials such as cloned genes, DNA probes, and human chromosome libraries. The facilities include the American Type Culture Collection (ATCC); the National Disease Research Interchange (NDRI); a cephalopod resource; the Caenorhabditis Genetics Center (CGC); a sea snail resource facility; the Yeast Genetic Stock Center (YGSC); the Repository of Human and Mice DNA Probes and Human Libraries located at the ATCC; and the National Cell Culture Center.

C. elegans Research

During FY 1991, the BMMRP continued its support of the Caenorhabditis Genetics Center (CGC). The CGC currently maintains more than 1,550 mutant strains of Caenorhabditis elegans and has distributed over 1,290 strains to the research community this past year. C. elegans, a nematode, has been adopted as a model proving ground for gene sequencing by the Human Genome Project, and has a variety of biomedical research applications. Strains of this tiny roundworm are already being used by hundreds of researchers, including geneticists, neurobiologists, developmental biologists and environmental toxicologists.

The BMMRP not only provides core support for established centers, such as the CGC, but also supports projects to develop new biomaterials and conferences to disseminate information. The Program currently supports an effort to provide C. elegans researchers with a genetic toolkit. In particular, investigators are developing a set of chromosomal balancers covering the entire genome of C. elegans. Genetic stocks of C. elegans are expected to help in isolating and mapping mutations in any part of the C. elegans genome.

One group of investigator-users of the CGC facility reported that the millimeter-long C. elegans may be effective in environmental monitoring for mutagenic chemical pollutants. Researchers used a mutant strain of partially paralyzed worms, and found that mutagenic chemicals triggered genetic changes in paralyzed worms that resulted in motile progeny. This work suggests that this multicellular organism, which ordinarily lives in soil, could prove to be an equally effective biomonitor for soil, water, and air contamination.

Other scientists reported in 1991 on C. elegans as a potential model system for the study of aging. They discovered that a mutation in one of the genes controlling aging in C. elegans resulted in a 65 percent increase in the roundworm's mean life-span and a 110 percent increase in its maximum life-span. This same mutation apparently was also responsible for a five-fold decrease in the number of progeny produced over the life of the organism. These and related studies are expected to give geneticists clues about the contribution of individual genes to the normal and pathologic aging of humans.

The National Disease Research Interchange

The National Disease Research Interchange (NDRI), another BMMRP-supported resource, procures and distributes a large variety of normal and diseased human cells, tissues, and organs to researchers interested in studying human systems directly.

The processes that lead to long-term complications of diabetes mellitus are not well understood; however, there is evidence that chronic hyperglycemia is a major factor in the development of many diabetic complications. Diabetic and nondiabetic arterial tissues, provided by NDRI, were used by researchers who are investigating the long-term effects of sustained hyperglycemia in patients with diabetes. These investigators have shown that excessive accumulation of glucose-derived products occurs in the arteries and circulation of diabetic patients and this increase parallels the severity of renal impairment in these patients. Strategies to prevent or improve the clearance of these products may help improve the life expectancy of patients with end stage renal disease.

The NDRI continues to provide pancreatic tissue needed to isolate islet cells for human transplantation and clinical trials. The major objective of islet transplantation is to transplant functional insulin-producing cells into patients with insulin-dependent diabetes mellitus (IDDM). Thus far, five IDDM patients who have undergone islet transplantation have achieved insulin independence from 1 to 9 months, with one patient who has been insulin independent for over one year.

BMMRP continues to be the focal point for activities involved with the Congressional intention to reduce or replace vertebrate animals in research. BMMRP also provides core support for the Center for Alternatives to Animal Testing (CAAT) which develops in vitro alternatives to the use of whole animals in evaluating drugs or products. CAAT is involved in many activities in the area of validation and technology transfer including organizing an international symposium on alternative methods in toxicology, conducting technical workshops on cell culture testing systems, and publishing technical reports and newsletters.

National Center for Research Resources

Research Centers in Minority Institutions

Authorizing Legislation - Sections 301, 479, 480, and 487 of the Public Health Service Act. 1993 Authorization: Indefinite.

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$22,090,000	$23,574,000	$23,574,000	---

The Research Centers in Minority Institutions (RCMI) Program objective is to expand the Nation's capacity for research in the health sciences by assisting, through grant support, predominantly minority institutions that offer the doctorate degree in the health sciences or health-related sciences to improve their research infrastructure. To date, seventeen institutions have received awards. The grantees include three colleges of pharmacy, seven medical schools, six graduate schools and one school of veterinary medicine. They are located in the states of Hawaii, California, Texas, Louisiana, Tennessee, Georgia, Alabama, Florida and New York, as well as in Puerto Rico and Washington, D.C.

In FY 1989, supplemental awards were made to develop a research infrastructure for AIDS and AIDS-related research, since AIDS has a disproportinate effect on minority populations. The National Institute of Allergies and Infectious Diseases (NIAID) cofunded this initiative and will continue to do so. This support mechanism will enable RCMI grantees to make major contributions in research on the AIDS virus.

In FY 1990 NIAID's involvement with RCMI grantees was expanded to develop the research infrastructure to participate in AIDS clinical trials. NIAID made three awards to facilitate RCMI involvement with the national network of AIDS Clinical Trials Groups - a network of 47 institutions that conduct AIDS clinical trials.

Funding for the Research Centers in Minority Institutions during the last 5 years has been as follows:

	Amount
FY 1988	$11,010,000
FY 1989	15,312,000
FY 1990	17,503,000
FY 1991	22,090,000
FY 1992	23,574,000

Rationale for the Budget Request

The FY 1993 budget request for the Research Centers in Minority Institutions budget activity is $23,574,000, the same as the FY 1992 estimate.

Fabry's Disease

RCMI-funded scientists made progress during 1990 toward developing a treatment for the rare inherited disorder called Fabry's disease. Fatal in early or middle adult years, Fabry's disease is an inborn error of metabolism characterized by a deficiency of the enzyme alpha-galactosidase A, which makes it impossible for the body to metabolize many carbohydrates and lipids that then accumulate in the tissues, causing excruciating pain. Until now, enzyme replacement therapy was not a promising approach, because of an inadequate supply of the missing enzyme. However, after an RCMI-funded scientist isolated the human gene coding for alpha-galactosidase A, recombinant DNA technology has made the enzyme available in virtually unlimited quantities.

Hypertension

Different results were observed for men and women when investigators studied the combined impact on blood pressure of caffeine and a mental arithmetic stress test in healthy young black and white men and women. In the first study 40 black and white men who were regular coffee drinkers were studied; 20 of them -- 10 of each race -- had a family history of hypertension but all had normal blood pressure. The men received two doses of caffeine or placebo in a double-blind study. Blood pressure and heart rate were subsequently measured, and the arithmetic stress test was administered.

After caffeine administration the men had higher blood pressure than after placebo administration, but racial and family history differences did not affect the results. Mental stress and caffeine had an additive effect on blood pressure. Young black men with a family history of hypertension were slower to recover their normal blood pressure than were white men with a similar family background. Heart rates were higher overall among whites than blacks, but this difference was unrelated to caffeine or the mental stress test. When comparable testing was conducted among 48 normotensive black and white women who were not regular coffee drinkers, caffeine increased the blood pressure only during periods of mental stress. As with men, caffeine had little effect on heart rate, and the effect on blood pressure was unrelated to race or a family history of high blood pressure. The studies are part of a larger program to investigate why blacks are at a disproportionately higher risk of hypertension and its consequences than are whites and other population groups.

Pain Research

During the past year neurophysiologic studies were conducted of the transmission of painful sensations received by nerve cell receptors in an area of the spinal cord called the medullary dorsal horn, a nerve center that influences sensory information affecting the face. The neurophysiologists conducted their research with anesthetized rats that were given various compounds that blocked or, in some cases, heightened the sensation of pain caused by extreme heat. Dynorphin, a naturally occurring opioid compound, reduced the input of painful signals caused by a heat stimulus at some of the receptors in the dorsal horn; in other cases it increased the thermal effect, and in still others it had a biphasic effect.

An experimental synthetic opioid compound reduced pain sensations in the superficial layers of the dorsal horn; however, deeper in the dorsal horn the responses of multireceptive nerve cells were variously reduced or enhanced. The scientists are continuing their studies of multireceptive nerve cells in the dorsal horn and ways in which pharmacologic agents affect the sensation of pain.

Human Genome

In FY 1992 and 1993, the scope of the Program will continue to be expanded in order to facilitate the participation of RCMI grantees in the achievement of the goals of the various NIH Institutes, Centers and Divisions (ICDs). In FY 1991, plans for expanding the scope of the Human Leukocyte Antigen (HLA) laboratory at Howard University, which has been supported by the RCMI Program since 1985, was initiated. Support for this expansion was provided collaboratively by the National Center for Human Genome Research and the RCMI Program. The long-range objective is to create a resource of reference families from the African-American population. It is anticipated that this resource would be of benefit to the Human Genome Initiative by providing additional human pedigrees to be used in linkage analysis. In addition, linkage maps generated using this resource of African-American families could be compared with the linkage map currently being generated for Caucasians to determine the potential for population differences.

National Center for Research Resources

Research Facilities Improvement

Authorizing Legislation - Proposed

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
---	---	$12,000,000	+$12,000,000

In contrast to majority institutions, many of which were provided major support for renovations and construction up until the mid-seventies through the Health Professions Education Assistance Act, most minority institutions have not received major support from the Federal government for facility construction or renovation for conducting state-of-the-art biomedical research. Facility construction and/or renovation is critical to developing the research potential of these institutions.

This is the second year that funds have been requested specifically for a facilities development program at Historically Black Colleges and Universities and similar institutions. However, no funding was provided for the program in FY 1992.

Rationale for the Budget Request

The FY 1993 budget request for the Research Facilities Improvement budget activity is $12,000,000. These funds are requested to initiate a program of facility renovation and construction at Historically Black Colleges and Universities (HBCUs) and similar institutions.

In a report published in September 1990, entitled "Scientific and Engineering Research Facilities at Universities and Colleges: 1990:" the National Science Foundation identified facilities, especially available space for research, as an emerging impediment to the capability of minority institutions to perform research. Twenty-nine HBCUs, representing 81 percent of all Federal obligations to HBCUs for research and development, participated in the study.

The data clearly point out the discrepancy in the research space available at HBCUs as compared to the research facilities at U.S. colleges and universities. The relative ratio of research space at major research and development centers and HBCUs, in mean space per institution, in square feet is 800,000/49,700 or 16/1. Clearly, adequate research space has been a historical barrier to HBCU participation in research and development. These findings can be extrapolated to other minority institutions.

The new Research Facilities Improvement Program will enable the conduct of state-of-the-art biomedical research, so that these grantees can participate in clinical trials and become strong centers for research on diseases that disproportionately affect minority populations. This infrastructure development will directly and positively affect several NIH minority programs, as well as other NIH components which provide research funds to investigators at minority institutions. The effect of this program will eventually be felt across all NIH programs, in terms of expanded competitiveness and ability to conduct all types of biomedical research.

This effort will broaden the base of institutions that conduct research, targeting institutions that have had difficulty in the past obtaining construction funds from state, local and private sources. Institutions participating in this program will be required to obtain some funding from non-Federal sources, and consideration will be given to the amount of non-Federal funds that applicant institutions have secured to match NCRR funds. All grants will be peer reviewed prior to award.

National Center for Research Resources

Research Management and Support

Authorizing Legislation - Sections 301, 479, 480 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
98	$13,393,000	97	$13,639,000	97	$14,307,000	---	+$668,000

The Research Management and Support activity provides the resources and staff necessary for the program management and scientific direction of the Center and its seven extramural programs. Scientific and administrative staff work together to plan, develop and carry out these programs in order to provide the extramural research community with the resources essential for the conduct of biomedical research.

Administrative and managerial services are provided through the Office of the Director, the Office of Science and Health Reports, the Office of Science Policy, the Office of Grants and Contracts Management, and the Office of Administrative Management (including financial management, human resources management, and information resources management, as well as provision of general administrative services) to all components of the NCRR.

The extramural review staff provides policy direction and coordination for all phases of scientific and technical review activities within the NCRR involving research grants, research training grants, and research and development contracts. The extramural program staff provides the planning, development, administration and monitoring of the extramural research programs of the NCRR, and serves in a liaison capacity for applicants, grantees, other components of the NIH and the Department, advisory bodies, and other interested groups.

In addition, Research Management and Support funds include support for the Center's use of the NIH centrally furnished services supported through the NIH management fund, the DHHS/NIH general expense fund, and the NIH service and supply fund.

Funding for the Research Management and Support activity program during the last 5 years has been as follows:

	Amount	FTEs
FY 1988	$11,145,000	89
FY 1989	11,597,000	89
FY 1990	12,248,000	90
FY 1991	13,393,000	98
FY 1992	13,639,000	97

Rationale for the Budget Request

The FY 1993 budget request for Research Management and Support is $14,307,000. This represents an increase of 4.9 percent over FY 1992. Included in this request are built-in administrative cost increases, and a program decrease of $15,000. This level will support 97 FTEs, the same level as in FY 1992.

During FY 1993 continued emphasis will be placed on management improvement and operating efficiencies. The Center will monitor travel, printing, contractual services, and the purchase of supplies and equipment, while continuing to foster efforts in office automation and streamlined administrative procedures in order most effectively to carry out the Center's mission.

National Center for Research Resources

Detail of Permanent Positions

	1991 Actual	1992 Estimate	1993 Estimate
ES-4	1	1	1
Subtotal	1	1	1
GS/GM-15	7	7	7
GS/GM-14	15	15	15
GS/GM-13	6	5	5
GS-12	9	9	9
GS-11	8	8	8
GS-09	5	5	5
GS-08	3	2	2
GS-07	18	17	17
GS-06	10	9	9
GS-05	4	3	3
GS-04	1	1	1
GS-03	1	1	1
GS-02	1	1	1
Subtotal	88	83	83
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	0	1	1
Director Grade	7	7	7
Senior Grade	1	1	1
Senior Asst. Grade	0	0	0
Subtotal	8	9	9
Unfilled positions, end-of-year	0	0	0
Total permanent employment, end-of-year	97	93	93

NATIONAL INSTITUTES OF HEALTH

National Center for Research Resources

Advisory and Assistance Services

The FY 1993 Advisory and Assistance Services (AAS) estimate for the National Center for Research Resources is $260,000.

The contractual services estimate includes $234,000 for services obtained under purchase orders for advice and consultation in the following program areas: Laboratory Animal Sciences and Primate Research, Biological Models and Materials Research, Biomedical Research Support, Biomedical Research Technology, Clinical Research and Research Centers in Minority Institutions. Advisory and Assistance Services are additionally planned for the Office of Review and the Office of Science and Health Reports.

The FY 1993 estimate for compensation of National Advisory Research Resources Council members is $26,000.

In FY 1993, the increase required ($30,000) reflects the effects of inflation and the requirements of the programs under a stable budget.

Internal Controls

Policy guidelines exist in the form of OMB Circular A-120 and DHHS General Administration Manual 8-15. Each year a consultant services plan is prepared identifying planned AAS procurement. The NIH accounting system contains Common Account Numbers (CANs) that have been designated for use in identifying and aggregating costs for AAS.

WEDNESDAY, MARCH 25, 1992.

NATIONAL CENTER FOR NURSING RESEARCH

WITNESSES

DR. ADA SUE HINSHAW, DIRECTOR, NATIONAL CENTER FOR NURSING RESEARCH

DR. BERNADINE P. HEALY, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. JANET HEINRICH, DIRECTOR, DIVISION OF EXTRAMURAL PROGRAMS, NATIONAL CENTER FOR NURSING RESEARCH

WILLIAM RUSS, EXECUTIVE OFFICER, NATIONAL CENTER FOR NURSING RESEARCH

ROBYN STRACHAN, BUDGET OFFICER, NATIONAL CENTER FOR NURSING RESEARCH

DENNIS P. WILLIAMS, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTRODUCTION OF WITNESSES

Mr. STOKES [presiding]. The Committee will come to order.

Our first witness this morning will be Dr. Ada Sue Hinshaw, testifying on the 1993 budget for the National Center for Nursing Research.

Dr. Hinshaw, it is a pleasure to welcome you here this morning. If you would like, introduce who you have with you before you make your opening statement?

Dr. HINSHAW. Yes.

On my far left, Mr. William Russ, our Executive Officer; Ms. Robyn Strachan, our Budget Officer. On my immediate right, Dr. Janet Heinrich, Director of the Division of Extramural Programs; and Mr. Dennis Williams, Deputy Assistant Secretary for Budget, Department of Health and Human Services.

Mr. STOKES. You may proceed.

OPENING STATEMENT

Dr. HINSHAW. Mr. Stokes and Mr. Pursell, I am honored to appear before you to discuss the programs for the National Center for Nursing Research and the findings that have emerged a mere six years after our establishment.

We are beginning to see research questions turn into research results that promise effective interventions for nursing practice and for improving the health and well-being of the American people. Preliminary findings are appearing from clusters of studies in health promotion; the mitigation of the effects of disease and disability; and prevention and care of low birth-weight infants, one of the Nation's most pressing health problems.

In the interest of time, I will highlight but two of these NCNR-supported new findings. They relate to Alzheimer's disease and the side effects of cancer treatment.

As we know, life does not stop with the onset of a terminal illness. Patients with Alzheimer's disease, for example, increasingly have trouble speaking, cannot solve the simplest problems, and lose their memories. They often finish their lives in expensive nursing homes away from their families and friends.

Dr. Mary P. Quayhagen and her team at the University of San Diego have developed a very promising intervention that has the potential to delay costly institionalization by keeping these patients home longer, and improving the quality of life, both of the patients and the family members working with them.

Dr. Quayhagen is examining the use of mental stimulation exercises that can be administered by family caregivers for one hour each day. In her study, Alzheimer's patients that received these mental stimulation exercises showed improved mental functioning, whereas the control group showed the continual mental decline typical of this disease.

The intervention also helped family caregivers who reported a decline in physical symptoms—they felt better.

Caregivers also reported greater satisfaction and a higher quality of life despite the burden of providing this care.

Another threat to health is cancer and its frequently daunting treatment regimens. Life-saving or life-prolonging chemotherapy can induce side effects, such as nausea and vomiting, that can compromise life's quality and affect a patient's ability to continue treatment.

While seeking answers to this problem, Dr. Gary R. Morrow and his colleagues at the University of Rochester Cancer Center found that certain behavioral techniques, such as deep muscle relaxation, reduce chemotherapy side effects better than anti-nausea drugs alone. The techniques are taught to patients by nurses and other health professionals.

Preliminary findings indicate that these techniques may be used in different treatment settings and improve people's responses to these essential, but often uncomfortable or painful, weapons against cancer.

As answers continue to surface from a variety of studies, the NCNR has identified three program areas for emphasis during fiscal year 1993: normal processes in mid-life women; long-term care requirements of older people in nursing homes; and symptom management of patients with neurological disorders such as confusion.

Another important area is pain. The Agency for Health Care Policy and Research recently released practice guidelines for the Management of Pain. In the process of developing guidelines, several areas that need research were identified.

There is a need for research that will allow us to measure the intensity of pain more definitively, incorporating a cultural point of view. There is also a need for additional strategies to help with the management of the pain. Studies suggest a major problem with treatment of pain, both for children and adults. Apparently, we provide about 50 percent of the total pain medication that is needed. Yet having pain retards recovery and can give the sufferer very definitive physiological problems.

A study supported by the NCNR focuses on the effects of pain on children of African American, Hispanic and European-American backgrounds.

The goal of another NCNR study is the further development of the Oucher Scale as a clinical tool to measure pain intensity of children. Children need to use communication mechanisms other than words, because they cannot always tell us in words what they are experiencing. But they can point to a face on the Oucher Scale, which describes for them the same amount of pain they are feeling.

A nurse clinical investigator shows the Oucher Scale to a child in pain and asks the child to point to the face that describes the amount of pain he or she is feeling. As the child points to that particular face, the investigator is able to convert the response to a number on a zero to 100 scale. That number gives the investigator an indicator of the intensity of the child's pain.

The Oucher Scale has been in existence since 1983, but it has only been used with white or European-American children. At this point, the investigator we are supporting has developed the Oucher Scale for Hispanic and Black children.

The investigator is going forward to look at ways to manage the pain once she knows the level of its intensity.

In conclusion, I am pleased to report that clusters of studies of critical importance to health are either in process or are already producing usable results.

In 1993, we will continue to move research to the point we all wish to see, and that is better interventions and strategies for nursing practice, so that patients, families, everyone can maintain optimal health.

Thank you, Mr. Stokes and Mr. Pursell.

The 1993 budget request for this Center is $48,569,000.

I will be pleased to answer any questions.

[The statement of Dr. Hinshaw follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement of the Director
National Center for Nursing Research

Mr. Chairman, I am honored to appear before you again to discuss the programs of the National Center for Nursing Research and to share with you the excitement of research findings and opportunities that have emerged a mere six years after our establishment. We are beginning to see research questions turn into research results that promise effective interventions for nursing practice and for improving the health and well being of the American people. Preliminary findings are appearing from clusters of studies in health promotion, the mitigation of the effects of disease and disability, and prevention or care of low birthweight infants, one of the Nation's most pressing health problems. In the interest of time, I will highlight but two of these NCNR-supported new findings. They relate to Alzheimer's disease and the effects of cancer treatment.

As we know, life does not stop with the onset of a terminal illness. Patients with Alzheimer's disease, for example, increasingly have trouble speaking, cannot solve the simplest problems, and lose their memories. They often finish their lives in expensive nursing homes away from their families and friends. Dr. Mary P. Quayhagen and her team at the University of San Diego have developed a promising intervention that may help keep these patients home longer and improve the quality of the lives that remain to them. She is examining the use of mental stimulation exercises that can be administered by family caregivers for one hour each day. In her study, Alzheimer's patients that received these mental stimulation exercises showed improved mental functioning, whereas the control group showed the continual mental decline typical of this disease. The intervention also helped family caregivers who reported a decline in physical symptoms. Research like Dr. Quayhagen's has the potential to delay costly institutionalization and extend the time patients remain home with their families.

Another threat to health is cancer and its frequently daunting treatment regimens. Life-saving or life-prolonging chemotherapy can induce side effects, such as nausea and vomiting, that can compromise life's quality and affect a patient's ability to continue treatment. While seeking answers to this problem, Dr. Gary R. Morrow and his colleagues at the University of Rochester Cancer Center found that certain behavioral techniques, such as deep muscle relaxation, reduce chemotherapy side effects better than anti-nausea drugs. The techniques are taught to patients by nurses and other health professionals. Preliminary findings indicate that these techniques may be used in different treatment settings and improve people's responses to these essential, but often uncomfortable or painful weapons against cancer.

As answers continue to surface from a variety of studies, the NCNR has identified three program areas for emphasis during FY

1993: normal processes in mid-life women; long-term care requirements of older people in nursing homes; and symptom management of patients with neurological disorders.

Health issues of mid-life women will be emphasized because of the many poorly understood syndromes that occur during this time. They include musculoskeletal and gastrointestinal discomforts, fatigue, insomnia, weight gain, and vasomotor instability. These symptoms often cause women to seek medical care, miss work, and feel barred from living life to the fullest. Often there is no specific, observable pathology, leading physicians to label complaints as functional or psychosomatic, and prescribe psychopharmacological treatment that produces less than satisfactory results.

One study of mid-life women examines insomnia and poor sleep, which is said to affect from 15-30% of the general population, particularly mid-life women. Insomnia leads to impaired daytime function, contributing to cardiovascular disease and premature mortality. The purpose of a study by Dr. Joan Shaver at the University of Washington is to determine the types of insomnia in mid-life women and to develop related treatment strategies.

Long-term care requirements of older persons in nursing homes will be the second area of emphasis in FY 1993. As the U.S. population ages, there is an increasing proportion of people with disabilities, secondary to chronic illness, that produce functional limitations such as problems with walking or toileting. These limitations, rather than the primary illness, frequently require expensive residential care. NCNR-supported research in this area includes assessment of the severity of pressure sores, prevention of fractures through the use of hip pads, control of nighttime urinary incontinence, enhancement of functional and cognitive abilities, improved self-care, and continued participation in activities of daily living.

In FY 1993, NCNR's long-term care program will focus on physical problems requiring special care, such as dehydration, infections, depression, impaired functioning, and social isolation. The goal is to identify interventions to decrease physical dependency and cognitive impairment; preserve or improve functioning; facilitate self-care; increase involvement of family members; and enhance the patient's chances of discharge from nursing home to residence.

The third area of emphasis for FY 1993 is the management of neurological symptoms that result from stroke and other neurological disorders, brain injury, and treatments with toxic effects. These symptoms can range from memory loss, agitation, cognitive impairment, and disorientation, to balance problems that limit a person's functioning. They cause a number of major health-care problems while compromising the quality of life of the patient.

A current NCNR-supported study concerns neurological damage from whole brain radiation and chemotherapy in children. As more children achieve long-term remission from cancer and immunological disorders, knowledge about damage to the brain from treatment effects is increasingly important. The relationship of radiation dose and chemotherapy levels to central nervous system damage and cognitive impairment is being determined in children who are being treated for leukemia, brain tumors, and disorders requiring bone marrow transplants. Once this relationship is understood, children at risk for cognitive impairment may be identifiable, so that early interventions can help the child compensate or adapt to the changes in cognitive function.

Cutting across all three areas of emphasis and other NCNR-supported studies is concern for the health of vulnerable populations; that is, the minorities, the poor, residents of rural areas, women, children, and older people. Additionally, in collaboration with the National Institute of Child Health and Human Development and the Office of Minority Programs, the NCNR is participating in the planning and implementation of an initiative that targets infant mortality among minorities in Washington, D.C.

Many other important areas of research will continue to receive NCNR support during FY 1993. One such area is pain, which, according to one estimate, disables 50 million Americans yearly, ranging from a few days to many months at a time.

The NCNR is currently funding a cluster of studies of pain management in children and adolescents. One study focuses on the effects of two nursing interventions on the intensity of postoperative pain in 300 children of African-American, Hispanic, and European-American backgrounds. The interventions are based on activation of central pain control mechanisms, such as distraction and relaxation, and peripheral control mechanisms, such as holding or positioning, and warm and cold applications.

Studies of caregiving are also being emphasized. Data suggest that caregivers experience extensive physical, emotional, and financial costs as they cope with complex problems, day in, day out, sometimes for years, in caring for an ill or disabled person at home. Most of these caregivers, whether a professional or a family member, are women. The needs of the caregiver, the caregiving process, the outcomes for both patient and caregiver, and the role of ethnic differences, are also being investigated. The care recipients in these studies are adults or children with conditions such as Alzheimer's disease, cancer, cardiac disease, hip fractures, and AIDS.

An intramural study is focusing on women who care for elderly men with dementia in a cohort of Japanese-American families in Hawaii. Nurse investigators are assessing the ability of older women and working adult children to provide home care. Interventions and services which help these caregivers cope are also under study to determine their effectiveness.

Another NCNR research focus is on preventable health problems of children and adolescents. It is often during this period of life that unhealthy attitudes and habits related to diet, physical activity, alcohol and tobacco use, and sexual behavior, are formed. Not only do these risky behaviors have short-term repercussions, but they can spark the onset of chronic illness and cause premature or unnecessary death in the years ahead.

NCNR-supported studies develop and test models that promote health-enhancing behaviors in young people. The maintenance of a healthy lifestyle, popular today among an all too small segment of adult Americans, needs to be expanded to include our young and, ideally, everyone else.

The NCNR, in collaboration with the National Institute of Child Health and Human Development and the National Institute of Mental Health, initiated a request for applications in FY 1991 to establish multidisciplinary Exploratory Centers for Adolescent Health Promotion. Three of these Centers are now funded. The Center at the University of Michigan will study the relationship of cognitive factors to risk-taking or health promoting behaviors. At the University of Texas, Center investigators are studying the health behaviors of Mexican-American and African-American adolescents. The Center at the University of Kentucky focuses on rural youth.

One of the research priorities of the NCNR is studies of low birthweight, a primary risk factor for infant mortality and infant morbidity. The infant mortality rate in the United States, while decreasing, is still unacceptably high. Investigators are studying care procedures to improve the outcomes of low birthweight infants. In a cluster of studies, changes in feeding, positioning, and suctioning techniques are being tested. Findings from these studies indicate that both the time and energy required for these infants to recover from care procedures are reduced. As a result, the infants have increased weight gain and are more able to respond to their caregivers. At the same time research must be directed towards reducing the number of infants born each year below normal birthweight. Researchers are testing interventions with high-risk pregnant women to adopt healthy lifestyles.

Another strong research focus of NIH and NCNR is the HIV epidemic. NCNR is emphasizing clinical research on physiological and psychological symptoms during different stages of HIV infection. Interventions are under development to maintain optimal physiological and psychosocial functioning throughout the illness period, identify patient needs across different care settings, and characterize the progression of the disease.

The NCNR's intramural clinical research program focuses on the special health problems faced by people with HIV infection, their families, and their caregivers. Currently, the investigators are studying the causes, types and severity of nutrition-related problems, such as unintentional weight loss, decreased appetite, and malnutrition, and the effects of muscle weakness resulting from the drugs used to treat the HIV infection. The relationship between nutritional status and immune function is also being studied.

Through its research training efforts, the NCNR is developing a stable cadre of nurse investigators to address the complex problems related to improved patient care. Nurses, the majority of whom are women, need a variety of career options available to them to pursue a career in science. In FY 1991, NCNR supported 269 full-time training positions, the highest number since our inception. We are especially proud of our progress in supporting minority trainees by means of research and training supplements. This program began modestly in FY 1989 with 3 supplemental awards, and in FY 1991, 25 minority trainees were being supported. This past year NCNR was cited in The Scientist for aggressive and creative recruitment of minority colleagues by means of these supplemental awards.

In conclusion, I am pleased to report that the scientific vitality of nursing research is impressive, and it is increasing. Clusters of studies of critical importance to health are either in process or already producing usable results. In FY 1993, we want to continue to move research to the point we all want to see: better interventions and strategies for nursing practice so that patients, families, everyone, can maintain optimal health.

Thank you, Mr. Chairman. The FY 1993 budget request for this Center is $48,568,000. I will be pleased to answer any questions you may have.

Ada Sue Hinshaw, Ph.D, R.N.
Director, National Center for Nursing Research

May 20, 1939. Arkansas City, Kansas.

Education:
- B.S., University of Kansas, Lawrence, Kansas, 1961;
- M.S.N., Yale University, New Haven, Connecticut, 1963;
- M.A., University of Arizona, Tucson, Arizona, 1973;
- Ph.D., University of Arizona, Tucson, Arizona, 1975.

Professional History: 1963-1965, Instructor and Chairperson, Maternity Nursing Section, University of Kansas, Lawrence, Kansas. 1966-1967, Assistant Professor, School of Nursing, University of California, San Francisco, California. 1968-1971, Administrative Coordinator, First Year Undergraduate Program, School of Nursing, University of California, San Francisco, California. 1971-1975, Masters' and doctoral studies, University of Arizona, Tucson, Arizona. 1975-1987, Liaison Position: Director of Nursing Research, University Medical Center, Tucson, Arizona and Professor and Director of Research, College of Nursing, University of Arizona, Tucson, Arizona. 1987-Present, Director, National Center for Nursing Research, National Institutes of Health.

Professional Organizations: American Academy of Nursing, American Nurses' Association (ANA), ANA Council of Nurse Researchers, Arizona Nurses' Association, Sigma Xi, Western Society for Research in Nursing, Sigma Theta Tau, National Academies of Practice, Institute of Medicine

Honors, Awards: Kay Schilter Award, University of Kansas School of Nursing, 1961. Lucille Petry Leone Award, National League for Nursing, 1971. Wolanin Geriatric Nursing Research Award, University of Arizona College of Nursing, 1978. Sigma Theta Tau, Beta Mu Chapter, Award for Excellence in Nursing Education, 1980. Alumni of the Year Award, University of Kansas School of Nursing, 1981. Distinguished Alumni Award, Yale University School of Nursing, 1981. Nurse Scientist of the Year Award, American Nurses' Association, 1985. Elizabeth McWilliams Miller Award for Excellence in Research, Sigma Theta Tau International, 1987. Doctor of Science Degree, University of Maryland, 1988. Doctor of Science Degree, Medical College of Ohio, 1988. Doctor of Science Degree, Marquette University, 1990. Alumni Achievement Award, University of Arizona, 1990. Distinguished Service Citation, University of Kansas, 1992. Doctor of Science Degree, University of Nebraska, 1992.

NIH STRATEGIC PLAN

Mr. Stokes. Thank you very much, Dr. Hinshaw.

Dr. Hinshaw, will you need to revise your research agenda to accommodate the proposed NIH strategic plan?

Dr. Hinshaw. No. We have been involved since the beginning in the NIH strategic plan.

The NCNR research priorities are going to fit very nicely within the five objectives that are now outlined in the evolving NIH strategic plan. The NIH plan also provides us with some additional opportunities that we have badly needed.

For example, Objective 1, which looks at critical science and technology, will allow us to expand a biological studies initiative that will be important for nursing practice.

Nurse scientists tend to be very strong in the psycho-social aspects of research, but not as strong in the biological aspects.

The National Nursing Research Agenda priorities fit nicely within the second objective of the NIH strategic plan on research capacity. For example, Prevention and Care with Low Birthweight Infants, NCNR, fits with Child Health and Infant Mortality, NIH; Long-Term Care of Older Persons, NCNR, fits with Chronic Illness and Aging, NIH.

I could give you other examples.

Mr. Stokes. When will you implement all seven parts of your research agenda?

Dr. Hinshaw. The first two priorities have been implemented in 1990 and 1991—low birthweight and prevention and care of HIV infection.

For example, in 1986 we had less than $500,000 invested in prevention and care of low birthweight infants. In 1993, we will have $6,400,000, and some 30 studies clustered in this area.

It allows us to be very active in the Washington, D.C. infant mortality and low birthweight initiative.

We have had a very good response. We intend to evaluate the success of our efforts to focus on these research priorities.

Mr. Stokes. You plan to hold a conference next year to develop five new sections for the research agenda. Are you at all concerned about spreading your resources too thinly?

Dr. Hinshaw. We have used the national agenda as a way of targeting critical health problems on which we feel nursing can make an impact.

By 1995, we will have completed the first seven research priorities. In that same year, 1995, the next five will move into place to carry us from 1995 to 2000. It is planned to put forward one research priority a year.

RESEARCH PROJECT GRANTS

Mr. Stokes. Dr. Hinshaw, your 1993 budget supports the largest number of new grants in your Center's history. Are you now focused on stabilizing the portfolio rather than expansion?

Dr. Hinshaw. Fifty-three new grants is larger than ever before. It was usually 48 or 50.

But it represents a success rate of only 15.5 percent. The NIH success rate is 26.4 percent. So we are still focused on expansion of the NCNR portfolio.

INSTITUTE STATUS

Mr. **Stokes**. Dr. Healy has announced that she is proposing to administratively convert your Center to an Institute. Will Institute status create additional administrative costs?

Dr. **Hinshaw**. There is no additional money needed for the conversion to institute status. We appreciate Dr. Healy's support of that change. We feel it is a legitimization of nursing research.

There will be no additional funds needed for this unless one looks at something like stationery, and I think we can handle that.

DOWNWARD ADJUSTMENTS OF GRANTS

Mr. **Stokes**. How are you dealing with the issue of downward adjustments of grants in 1992 and 1993?

Dr. **Hinshaw**. Very carefully and individually. Each competing award is looked at separately.

Downward adjustments range from zero to upwards of 15 percent. In 1991, we averaged about 11 percent for downward adjustments.

There is, however, very good stability for noncompeting grants going into their second year, with only a 4 percent increase allowed for recurring costs as specified under the NIH cost management plan. There is no further downward adjustment on noncompeting awards.

RESEARCH CENTERS

Mr. **Stokes**. What is your current mix of specialized and exploratory research centers?

Dr. **Hinshaw**. We have two specialized and five exploratory centers in place.

We have used the exploratory centers for schools which are on the cusp of becoming research intensive and need additional help to apply for RO1's or to become specialized centers.

The exploratory centers are addressing very important areas of substantive nursing practice.

For example, at the Universities of Texas, Kentucky, and Michigan, very important studies are being conducted that target the health promotion decisions young people make about alcohol, tobacco, and exercise.

Mr. **Stokes**. How many more years do you expect to need the exploratory center mechanism?

Dr. **Hinshaw**. The advisory council is suggesting that we continue with the exploratory center mechanism until 2000. In addition the advisory council suggests that we need to expand the specialized centers.

Mr. **Stokes**. What size centers programs are you targeting?

Dr. **Hinshaw**. The direct costs of the specialized centers are about $350,000. They should probably grow to $500,000.

We are not envisioning huge centers programs, but rather programs that provide core support to large clusters of RO1's.

RESEARCH TRAINING

Mr. STOKES. The share of your budget allocated for research training is almost triple the NIH average. Why is training such a high priority?

Dr. HINSHAW. As you know, we have been in existence about six years. The discipline is rapidly growing. We need to have a cadre of nurse scientists. Getting people prepared through pre- and post-doctoral programs has been a priority initiative for us. The National Academy of Science has recommended that we provide in research training funds for 320 people annually. We have only been able to reach 269 in FY 1991. In FY 1993, we are projecting 245, so we have a distance to go.

Mr. STOKES. If you had the flexibility, would you consider transferring funds from research grants to training?

Dr. HINSHAW. That is a real dilemma. I have talked about it with the advisory council and the National Nursing Associations, trying to find a balance between the low success rate we have in terms of RPGs and the numbers we have in training.

At this point, I would probably not move any money into research training given the current budget.

Mr. STOKES. Since your training has been underway for several years, have you begun to increase emphasis on post-doctoral training?

Dr. HINSHAW. Yes. We have moved from only two institutional awards in the field to 16. They are placed with schools of nursing in which there are cadres of individuals conducting research.

These schools are where we are getting the most rapid increase in post-doctoral study. We have moved from 13 or 14 people in post-doctoral programs a few years ago to around 40 at this time.

If we count career awards, it is over 50. We plan to continue the post doctoral emphasis.

Only about 15 percent of our training awards are in post-doctoral study. We would prefer to see that at about 35 to 40 percent.

AIDS RESEARCH

Mr. STOKES. What percentage of your in-house research is directed toward AIDS?

Dr. HINSHAW. In terms of AIDS, we have $3,400,000 in FY 1993. That accounts for only about 7 percent of our research portfolio.

We do have our intramural research program, which is targeted to HIV infection.

We have difficulty, as other fields have had, generating a number of projects focusing on physical care issues of HIV infection—myopathy, muscle wasting, and the side effects of the very powerful drugs. We have started the intramural program in order to fill that gap, and now have the research under way focusing on the physical care problems of nursing practice.

INTRAMURAL RESEARCH PROGRAM

Mr. STOKES. In the long run, will your in-house research remain a small part of your overall program?

Dr. HINSHAW. The program is planned for growth. We indicated in last year's hearings that that is where most of our FTE growth would be.

We hope to maintain the program in an interdisciplinary fashion. In other words, we do not see ourselves building new research laboratories or clinical resources to conduct our research.

Instead, we are working side by side in an interdisciplinary manner with our biomedical colleagues and are using the existing infrastructure for our nursing research. We are developing very important nursing protocols from this approach.

Mr. STOKES. Thank you, Doctor.

Mr. Pursell, I yield to you.

GROWTH OF NCNR

Mr. PURSELL. I thank you, Mr. Stokes.

Our good Chairman is next door at my other committee presenting the Kentucky delegation's proposals for Water Projects. Let the record show that he is working hard for his home State.

Dr. Hinshaw, can you tell me how the nursing research center has matured and grown?

Are we in a transition to the Institute now?

Even though the law has not been signed, I know the Pursell amendment is moving through Congress.

Dr. HINSHAW. Thank you for that.

Mr. PURSELL. Give us an assessment of where you think the nursing community is.

Dr. HINSHAW. It has been a very exciting six years at the National Center. We started with about $11,000,000 for research and research training. We are now defending a budget of more than for $48,000,000.

That is very rapid growth in that amount of time. The most important thing is to see the cadre of scientists growing rapidly and the number of universities that are able to support research in this area.

We have a body of knowledge now in which we are beginning to see some clusters of studies, such as the low birthweight cluster of studies. The knowledge is now there to understand culturally-sensitive prenatal care issues—how to attract women into prenatal care and retain them. We are beginning to use that information in projects like the D.C. initiative.

Mr. PURSELL. You have a role in that D.C. project?

Dr. HINSHAW. Yes, sir. We are working with the National Institute of Child Health and Human Development, and we are looking at the D.C. community programs. We want to see why there is such a high rate of infant mortality in D.C. Then we will test culturally-sensitive interventions to try to bring those statistics down.

Mr. PURSELL. Where do you think the Institute will be in your strategic plan in terms of budgeting and personnel in five or ten years?

Dr. HINSHAW. I think we are on a fast track. We have had excellent support from NIH, and from Dr. Healy. When you consider the breadth of information needed for nursing practice and the fact that we have been in existence only six years, an eight percent increase over our particularly small budget base is not a lot of money. If you convert that to actual money, we came through with only about $1,300,000 above current services or about nine grants. So the difficulty is continuing to build until that base gets large enough to support the breadth of needed nursing research.

WOMEN'S HEALTH INITIATIVE

Mr. PURSELL. How is your relationship with Dr. Healy's Women's Health Initiative Program?

Are you effectively involved in that? Could you identify some of your involvement?

Dr. HINSHAW. One of our 1993 initiatives within the Center will be targeted to women's health, particularly to mid-life processes.

We want to look at the complexities surrounding mid-life; such as, helping women overcome sleeplessness, GI irritability, muscle pain, and other typical phenomena that appear at this period of life.

These are often nebulous syndromes so women go to physicians not understanding what is happening and not able to articulate their problems well. There is no good knowledge base for how to react to this symptom complex.

Another aspect of womens health we are involved with is the emphasis on health promotion decisions that have to be made at mid-life. Women must make decisions about estrogen, calcium, and exercise. All of this has to be made for the prevention of cancer, heart disease, and osteoporosis, which is central to the NIH Women's Health Initiative.

So, yes, we have been very involved in helping to work with that particular initiative.

Mr. PURSELL. Dr. Healy, does the Women's Health Initiative have its own strategic plan?

Dr. HEALY. The Women's Health Initiative is part of a strategic focus the NIH has identified on the health of women, minorities and neglected populations. The Women's Health Initiative is one part of a broader strategy to address that issue.

The Women's Health Initiative, which Dr. Hinshaw talked about, involves 10 or 11 Institutes; the granting process and contracts will be filtered back through the Institute so all the money is a line item in the Office of the Director and it will be expended through the Institute mechanisms.

Mr. PURSELL. But in the strategic plan the Women's Health Initiative will not by itself have its own strategic plan?

Dr. HEALY. I think each of the Institutes has recognized that part of their mission has to be to look at it in a strategic way the health of women, minorities and underserved populations. Virtually all the principles of the plan should, and must, be adopted by every Institute.

They developed them. They were developed by the community of NIH leadership. Those are not only trans-NIH but are incorporated into the individual thinking of every Institute.

Dr. HINSHAW. These initiatives provide very exciting opportunities for all of us to do collaborative research together and pool our strengths and resources in many ways.

NURSING SHORTAGE

Mr. PURSELL. Let me ask you about the status of the nursing community. When I was on this Committee years ago, Secretary Califano said we had no shortage of nurses. This was 1978, 1979 or 1980, somewhere in that period.

They were using data from 1972. Is the nursing community doing any research in terms of the shortage of nurses and the need for nursing professionals?

Dr. HINSHAW. There are studies that have gone forward, thanks to those of you who have been vigilant. Those are conducted through the Health Resources and Services Administration, through their Division of Nursing.

After the two Commissions on Nursing, of which you were instrumental in being sure one of them moved forward, there was a recommendation of the kind of study that needed to be ongoing and conducted at so many year intervals; I don't have the details on that.

We are currently cosponsoring a study with the Division of Nursing in which they are looking at the number of nurse practitioners and clinical specialists. These types of positions seem to be the fastest growing in terms of demand, but not necessarily in terms of people to fill the positions.

The study will pinpoint clinical nurses and nurse practitioners by activities. The results should be ready for review in January of 1993.

NIH STRATEGIC PLAN

Mr. PURSELL. In the strategic plan, do you have a chance to have an input from the various nursing groups around the country?

I know Dr. Healy has been doing some public marketing of the strategic plan. Do you have some outreach type programs?

Dr. HINSHAW. Yes. You are talking about the evolving NIH strategic plan?

Mr. PURSELL. Correct.

Dr. HINSHAW. We have had a number of nurses at the meetings where the strategic plan has been discussed. It is an evolving plan, as Dr. Healy suggested.

Nurses have had major input either sitting on the panels or being active in the conferences.

Mr. PURSELL. What are they saying? Are they supportive? Is there honest criticism, a chance to offer alternatives?

Dr. HINSHAW. I think you just walked into my next comment. I discussed the Strategic Plan at a meeting of the National Nursing Research Roundtable.

The Roundtable has representatives from each of the major nursing organizations—ANA, AACN, NLN—all our major organizations. After an hour or so of discussion, they continued to be very excited about the strategic plan. They are all writing letters in support of the plan to Dr. Healy.

Yesterday I had a nurse scientist in the office who said, "I just want you to know I can see nursing foot tracks through each one of those areas of the strategic plan just as I can see the others."

As Dr. Healy indicated, we were each very much involved. We sat on the panels and wrote the words. I think that has come across.

SPACE ALLOCATION FOR NCNR

Mr. PURSELL. I have toured your facilities and I think that you are on the right track.

Are you out of space out there?

Dr. HINSHAW. We could never admit to having enough space. Recently, we have had support to double the space.

We will be one of the first groups to move into the new Natcher Building. We have had excellent support.

Mr. PURSELL. Thank you very much.

I have enjoyed working with you.

Dr. HINSHAW. Many thanks to you as well.

Certainly we want to say to Mr. Pursell many, many thanks for your championing of our causes. I know you have made your history in Congress, but certainly you are one of the major players in helping shape nursing research. Nursing practice in the long run will be much, much better for what you have done for us.

Mr. PURSELL. Thank you for your comment.

Dr. HINSHAW. I hope you don't have to be ill and experience any nursing care. However, you have had a large hand in improving nursing practice in this country.

Mr. PURSELL. The nursing community has helped me politically, especially at the University of Michigan. At that time, the nurses were complaining about shortages.

They came to my town meetings and I guess it became love at first sight. It has been a real honor to work with you and all your colleagues in the nursing community.

I wish you the very best and you, Dr. Healy, too.

WOMEN'S HEALTH

Mr. STOKES. Let me ask a few of my own questions at this time. Then, I will return to the Chairman's questions, if we have time.

I see NCNR has an 8 percent increase, and you did discuss that with Mr. Pursell a few moments ago, in the sense that there is little over $1,000,000, so it was not that much of an increase.

You might share with other Institutes as to how you got such a nice increase. Some of them, I am sure, would like to know what the strategy was for that.

Moving on, what type of studies does NCNR support that address normal physiological and psychological processes in mid-life women?

Dr. HINSHAW. We have almost 20 percent of our budget in the area of women's health. We have a specialized center dedicated to that research.

The Center primarily focuses on normal mid-life processes and the symptoms I talked about earlier, such as changes in sleep patterns and GI irritability. The Center is attempting to look at what the symptoms are and then develop some interventions for managing them.

There are other studies for colorectal screening for women and men. Some of our studies focus on helping healthy women make decisions about estrogen replacement.

We know that one third of the women who get a prescription for estrogen from a physician never fill the prescription. We know another third will stay with the prescription only one or two months. And we know the other third doesn't last beyond the average of one to two years.

How do we help them think through the use of estrogen in terms of long-term quality of life and the risks they may run later in life?

If they are not going to stay with estrogen prescriptions, how do we get them to participate in exercise programs, take additional calcium, and do other things to promote their own good health?

INFANT MORTALITY/LOW BIRTHWEIGHT

Mr. Stokes. As you know, infant mortality and low birthweight remain a major public health concern. Despite our efforts in this area, unacceptably high levels of low infant birthweight and infant mortality persist. What efforts are underway by NCNR to work on the problems of low birthweight and——

Dr. Hinshaw. We have an entire set of studies focused on prevention of, and care for low birthweight infants. These include understanding a particular ethnic group's perceptions, finding out what kind of dietary patterns are needed, then working within each ethnic and cultural nutrition system to increase healthy behaviors and keep people in the health care system.

We have a particular study being done in Hawaii with Hawaiian women in rural areas. They tend to seek prenatal care very late in the pregnancy.

This study is showing a change in that particular trend. Nurse practitioners have made use of the routine prenatal care system of course, but in addition to that, they have used the family network among women, which is so important in the Hawaiian culture. This network is called the "Coconut Grapevine."

In the neighborhoods, there is a Coconut Grapevine of women talking to each other two to three times a day; passing along information on how to make healthy decisions, how to set up meals, being sure one person knows she needs a certain kind of exercise.

The nurses literally are training women in that grapevine to pass on prenatal information. So in supplementing the system in that way, they are seeing the difference in when and how the women are coming in for prenatal care and following prenatal advice.

Mr. Stokes. What type of funding are you putting into this area?

Dr. Hinshaw. It is about 13.2 percent of our budget, about $6,400,000 for 1993.

Mr. Stokes. How does that compare to fiscal year 1992?

Dr. Hinshaw. In 1992 it was $6,000,000. So there is a slight increase.

HEALTH PROMOTION AMONG CHILDREN AND ADOLESCENTS

Mr. Stokes. On adolescent studies, I note in your budget justifications that the Center has initiated a research program concerning health promotion among children and adolescents. What type of activities are being supported in this area?

Dr. HINSHAW. Let me say, first of all, that this is one of the seven major priorities of the NNRA. In order to prepare researchers to move into a larger arena, we have funded three exploratory centers. One focuses on rural youth in Kentucky, looking at areas where there is a high prevalence of tobacco and alcohol use. Researchers are studying how this use affects young people's decisions, and how to turn young people around from choosing risky behaviors.

There is an exploratory Center at the University of Michigan looking at alcohol, exercise and smoking in terms of helping young people make healthy choices. If any of us had changed some of our behaviors back when we were 8 to 12 years old, as opposed to doing it later in life, we might be healthier today.

Mr. STOKES. Is any of this program targeted specifically to underserved or specifically minority groups?

Dr. HINSHAW. The Center at the University of Texas is targeted at Hispanics, and the one at the University of Michigan is targeted at African Americans.

BIOETHICS RESEARCH PROGRAM

Mr. STOKES. I note that NCNR has a program of bioethics. Can you tell us what types of problems the investigators are addressing in this bioethics research program?

Dr. HINSHAW. We are concentrating on an initiative in clinical bioethics. We are interested in the decisions people are making.

For example, one of the studies focuses on parental decisions for the care of premature infants in the neonatal intensive care units.

We need to understand how the parents are involved in these decisions; what goes into their decision process; what their worries and concerns are; and how we can help guide them in terms of information they need.

Another area is the management of pain. We understand that there is a major problem with the undertreatment of pain. I spoke for a few minutes about that earlier.

One of our studies is surveying 1,000 critical-care nurses to understand what are the dilemmas involved in their thinking process as they make decisions on assessing patient's pain and how much medication to give.

There is a dichotomy between what the person is suffering, on the one hand, and a nurse's concern that if too much medication is given, there may be side effects or even addiction.

Mr. STOKES. I was very impressed with the photographs you sent up here; the sensitivity that it displayed in your Center in the sense that children in particular, but also adults, can better identify with their own grouping as opposed to trying to identify pain of someone else. That showed some real sensitivity.

I think you should be commended for that.

Dr. HINSHAW. Thank you.

We will pass that on to the investigator as well.

CAREGIVING RESEARCH

Mr. **Stokes**. On caregiving research, as you know, caregiving places burdens on both patients and family members who provide care. To what extent do caregivers experience problems in care for the elderly?

Dr. **Hinshaw**. Caregivers bear high costs in terms of their own health, as well as extensive financial costs. We are supporting a series of studies that look at caregiving relationships and how to ease the burden and increase the quality of these relationships.

There are some abusive relationships that we are very concerned about. There is another set of studies that are looking at interventions nurses or health care providers can teach the caregiver that will help make the caregiver's situation more comfortable, as well as help the patient.

A good example of this is active mental stimulation used by Dr. Mary Quayhagen and taught to caregivers. Active mental stimulation techniques enable caregivers to better orient the patient. The patient loses memory at a slower rate.

One of the qualitative outcomes from the study was expressed by a caregiver who said, "I didn't realize they the (patients) could still do those types of things."

Dr. Quayhagen's study has the added dimension of decreasing the burden and improving the quality of life for caregiver and patient.

Mr. **Stokes**. Thank you, Ms. Hinshaw.

Now I want to yield back to the best Chairman in the Congress.

Mr. **Natcher** [presiding]. Mr. Pursell, I yield to you.

Mr. **Pursell**. Thank you, Mr. Chairman, I'm finished.

INTRAMURAL RESEARCH INVESTIGATORS

Mr. **Natcher**. Tell us, how many of your in-house research staff are investigators?

Dr. **Hinshaw**. At this point in the intramural program, we have two senior investigators and we have three research nurses working with the intramural projects.

In the extramural program we have 12 nurse scientists administering extramural research grants.

COLLABORATIVE RESEARCH

Mr. **Natcher**. How much additional funding do your research projects receive from other efforts with other Institutes?

Dr. **Hinshaw**. We have slightly over $2,000,000 that we leveraged upwards for nursing research.

RESEARCH TRENDS

Mr. **Natcher**. What are the recent trends in applications for your Center and what are you projecting for 1993?

Dr. **Hinshaw**. In 1991, we had a slight drop in the numbers of applications. That was the first time we had seen a drop since the creation of the Center. It was not just our Center but across NIH.

In 1992, we have projected a total of 319 applications, and in 1993, a total of 343. In 1992, as we look at both the routine applications coming into the system and those we anticipate will come in through RFAs, we expect to receive the number we projected.

RETIREMENT OF CARL PURSELL

Mr. NATCHER. Dr. Hinshaw, we want to thank you for your appearance before the Committee at this time in support of your budget request for 1993. It has been a good hearing.

Dr. Healy, the hearings all down through the weeks have been excellent with NIH. I want you to know.

You have heard me say on more than one occasion it is a pleasure to sit up here and listen to your people. They are well qualified. These people know what they are doing. It is a pleasure to sit here and hear the request presented each year.

I think at this time I ought to say this in the record. As you know, our friend, Carl Pursell made an announcement yesterday that we did not approve of, Carl Pursell is one of the best Members that we have in the House of Representatives.

He has been an excellent Member of the Appropriations Committee, down through the years, and especially on this subcommittee. I don't know who they will put in his place, but they will have some trouble making the change.

Mr. Pursell, I want you to know that we are going to miss you and we want to wish you the best of everything in the future. You have been good for your State.

You have been good for your district, and you have been good for your country.

Mr. PURSELL. Thank you.

Mr. EARLY. Would you yield?

Mr. NATCHER. Certainly.

Mr. EARLY. It is ironic that the Director of the Center for Nursing Research is here.

Dr. Hinshaw, it is a great loss for you. There has been no greater champion for nursing, and he is a very conservative guy. And, on NIH it was never Democrat or Republican. It was what was in the best interest of the people.

It has been a pleasure for me, Carl, to serve with you. Carl, you should reconsider.

Thank you, Mr. Chairman.

Mr. NATCHER. Mr. Stokes, I yield to you.

Mr. STOKES. Mr. Chairman, I had a chance yesterday afternoon after I heard about Carl Pursell's announcement, to tell him what a great loss I thought it was, not only to this committee, but to the Congress.

Carl Pursell is so highly respected on both sides of the aisle.

I have had a unique opportunity to work with him, as I did with Silvio Conte, on some matters across the line in which he has taken a special interest.

Yesterday morning in his absence, the NIH witness testifying about lupus talked about the amount of hard work that he has done in this area, along with me, to try to make some impact on a very debilitating disease.

Carl, I want you to know too that from my perspective, I want to concur with Joe Early, and ask you to reconsider.

You are going to be a great loss to us.

Mr. PURSELL. Thank you.

This is the greatest committee in the United States Congress. It has been a great love. We have a great staff.

NIH is the premier group in the country. I wish we could jump the $20,000,000,000. That is not even being conservative.

The Nation needs this great sort of agency, which is the world's premier leader under Dr. Healy, and all its professional directors.

It has been a wonderful experience, but it is time to pass the baton on and look at the flowers growing in my yard, and look at the tennis court, and do some other things, and keep my head high and walk out of the United States Congress with the feeling that we have had such a wonderful community and the committee leaders have been terrific.

I love this Committee. It has been a wonderful committee to me.

Thank you, Bill.

You and the staff have been wonderful.

Thank you.

Mr. NATCHER. Since March 4, 1789, we have had 11,384 men and women serve in the House of Representatives and the United States Senate. Out of that number, 691 of them served in both the House and the Senate.

Since I have been here, and I have been here a while, I think I served with 2,000 in the House and Senate. I keep a journal.

As you know, Dr. Healy, I am on volume 52. Dr. Healy, I want you to take care of yourself. I want you to read my journal.

I put it down just like it happened, not like you read it in the newspapers. I want Carl Pursell to know he comes out well in my journal.

Our Chairman Jamie Whitten sometimes stops me in the hall and says, "How am I doing in your journal?" Once I said last week, "You did not do too well."

Anyway, Carl, you come out well in my journal.

Doctor, we want to thank you and your associates for appearing at this time.

Thank you very much.

[The following questions were submitted to be answered for the record:]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

RESEARCH CENTERS

Mr. Natcher: Identify the number, type and subject area of your centers in 1992 and in the 1993 request.

Dr. Hinshaw: In FY 1992 the NCNR plans to continue support for two specialized research centers and five exploratory centers. The subject areas of the two specialized centers are: (1) Women's Health, which focuses on women's health issues across the life span and includes women of ethnic minorities and low income lifestyles; and (2) Advanced Care in Serious Illness, which focuses on three of the major goals of nursing care with patients who are seriously ill and their families--to enhance the outcomes of medical treatment, to enhance the quality of life if treatment fails, and to enhance wellness of families if death occurs.

Three exploratory centers originally funded in FY 1991 will be ongoing during FY 1992 and FY 1993 and focus on Adolescent Health and Behavior. Specifically, one center will focus on the health behaviors of Mexican-American and African-American adolescents; another will focus on rural youth; and the third will focus on the study of cognitive factors underlying the initiation and maintenance of health promoting and risk-taking behaviors among children and adolescents from different racial and socioeconomic backgrounds. The NCNR has recently issued an RFA for exploratory centers that target innovative clinical assessment and management strategies for symptoms commonly experienced by acutely or chronically ill patients. The remaining two exploratory centers will be funded from this RFA in FY 1992. Each of these seven Centers that are active in FY 1992 will be maintained in FY 1993.

ADVISORY AND AD HOC COMMITTEES

Mr. Natcher: How many advisory councils and ad hoc committees has your Center established?

Dr. Hinshaw: There is one National Advisory Council for Nursing Research that meets on a regular basis throughout the year to provide advice and second level peer review of research grant applications funded by NCNR. The Center has one standing review committee with primary responsibility for reviewing scientific merit of research training applications. Ad hoc review committees are created as required for special reviews related to NCNR initiated requests for applications. In FY 1991 there were two ad hoc review committees established for just such a purpose.

INTRAMURAL RESEARCH

Mr. Natcher: Your intramural research program is participating in the Honolulu Heart Program. Do you have researchers on site in Hawaii?

Dr. Hinshaw: One NCNR nurse researcher joined investigators of the Honolulu Heart Program and the Honolulu Aging Asian Study on site in January 1991. Her assignment was to plan and conduct a new portion of the Honolulu Aging Asian Study that would examine the impact on the caregivers (usually female family members) of dementia occurring in aging men. The goal of the NCNR study is to improve understanding of the burdens caregivers experience and the effect of the caregiving on the quality of the caregiver's life. The NCNR investigator provides oversight and expertise for the development and conduct of the NCNR study. Contractor personnel from the Kaukini Medical Center actually conduct the study.

WOMEN'S HEALTH

Mr. Stokes: How do the common health problems of midlife women relate to the Women's Health Initiative?

Dr. Hinshaw: Women now live out one-half of their adult years following the menopause, yet few studies have focused on women's health during this time. It has been shown that changes do occur in the thermoregulatory, metabolic, cardiovascular and hemostatic systems in response to a decline in ovarian hormones; yet the impact of these changes on health and disease is poorly understood. Reports of weight gain, gastrointestinal problems, musculoskeletal pain, fatigue and sleep dysfunction, depression and vasomotor symptoms such as hot flashes are common and often the major reason for women to seek medical care, lose work time and experience a decrease in health related quality of life. These symptoms are often treated with medications with less than effective results.

Wide gaps exist in the scientific knowledge base of the normal mid-life processes in a woman's life. These range from a better definition of the biologic, psychologic and socio-cultural determinants of those women who complete the menopausal transition without the need for interventions, the role of reactivity and stress responsibility in this population, the cultural and ethnic influences on mid-life minority women and how this may impact on their initiation or maintenance of health promoting behaviors in midlife, and the health effects of work (given that 74% of this population work outside of the home).

It has been argued that mid-life is an optimal time for prevention of adverse biological changes and for adoption of health-promoting behaviors that could have dramatic health effects in later years. But without a better understanding of these changes and behaviors, the opportunity to truly impact on this large and important segment of our population cannot be met.

The NIH Women's Health Initiative proposes to study the leading causes of mortality, morbidity, and declining quality of life in mature women in a three-part study: by measuring the effectiveness of hormone replacement therapy, dietary modification and vitamin supplements to combat heart disease, cancer and osteoporosis; by seeking effective ways to promote healthy behavior within local communities; and by screening a large population of women for signs of progressive diseases and predictors of future illnesses. This initiative also provides an opportunity to obtain information on health promotion behaviors in women, as well as ethnic and cultural differences in health seeking and health promoting behaviors and responses to treatment.

HEALTH PROMOTION AMONG CHILDREN AND ADOLESCENTS

Mr. Stokes: The Justification notes that the Center has initiated a research program concerning health promotion among children and adolescents. What type of activities are being supported in this area?

Dr. Hinshaw: The NCNR has three major thrusts with respect to health promotion among children and adolescents: exploratory centers, investigator-initiated research projects, and one of the priority expert panels under the NNRA. In addition, the NCNR is collaborating with other organizations within the NIH on the Minority Youth Health Behavior Research initiative.

Three multidisciplinary exploratory Centers for Adolescent Health Promotion were funded by NCNR as a result of a request for applications issued in collaboration with the National Institute of Child Health and Human Development and the National Institute of Mental Health in FY 1991. One of the centers, at the University of Michigan, is examining alcohol use, exercise habits, and smoking in terms of helping young people choose healthy behaviors; another center, at the University of Texas, will focus on the health behaviors of Mexican-American and African-American adolescents; and the third center, at the University of Kentucky, will focus on rural youth and examine the factors involved in the initiation and maintenance of tobacco use as well as attitudes and experiences with alcohol. Support for these centers allows institutions to facilitate collaboration among scientists from different disciplines with similar research interests and to fund preliminary studies which will lay the foundation for future independent research projects (R01s).

During FY 1992, the NCNR will convene an NNRA Priority Expert Panel to further delineate the research agenda in health promotion for children and adolescents. Eleven scientists from nursing, medicine, psychology, sociology, and anthropology will meet together to discuss the state of the science and identify research needs and opportunities for nursing. In order to ensure a coordinated effort, representatives will also be present from federal and private organizations with research programs in health promotion for children and adolescents, including the National Institute for Child Health and Human Development, the Centers for Disease Control, the Maternal and Child Health Bureau of the Department of Health and Human Services, the American Medical Association, the Carnegie Foundation and the Office of Technology Assessment. A document outlining the panel's deliberations will be published within the year and these recommendations will be used to outline future research initiatives.

Mr. Stokes: Why has the Center targeted children and adolescents as a priority population for health promotion studies?

Dr. Hinshaw: The NCNR has targeted children and adolescents as the priority population for its health promotion program because the nation's dominant preventable health problems result from behaviors rooted in the emerging lifestyles of young people. Attitudes and habits related to diet, physical activity, alcohol abuse, tobacco use, and sexual behavior are formed early in life. Health-compromising habits established at this time not only impact on the immediate well-being of young people, but also may persist into adulthood, with major long-range implications for the onset of chronic disease.

Mr. Stokes: To what extent will emphasis be placed on children of traditionally underserved populations?

Dr. Hinshaw: To date, emphasis has been placed on children of traditionally underserved populations in the exploratory centers funded by the NCNR and several of the investigator-initiated research projects. Two of the exploratory centers focus on the issues of health promotion among minority youth, specifically Hispanics and Black youth. A third center is looking at health promotion among rural youth. The NCNR has also collaborated with other organizations within the NIH in the Minority Youth Health Behavior initiative. Members of the upcoming NCNR Priority Expert Panel on Health Promotion among Children and Adolescents have expertise in the areas of minority health, rural health, and socially-disadvantaged populations, ensuring that research needs and opportunities in these areas will be identified for future research initiatives.

Mr. Stokes: For all the activities supported in this area, what level of funding is proposed in FY 1993? How does this compare to FY 1992?

Dr. Hinshaw: Under the FY 1993 President's Budget, the NCNR's research portfolio that focuses on health promotion among children and adolescents will be funded at approximately $2.5 million. This is an increase of $200,000 above the FY 1992 level.

MINORITY EMPLOYEES

Mr. Stokes: How many and what percentage of employees of your institute are minorities? Please provide a breakdown by race and grade level. How many are employed in a research capacity? To what extent are you recruiting minorities with graduate degrees in the area of nursing?

Dr. Hinshaw: Of NCNR's total of 48 full-time equivalent positions (FTEs), 12, or 25 percent, are occupied by minorities. Of NCNR's 13 senior research administrators at the GS-14/15 level, 3, or 23 percent, are minority. The intramural research program employs two research scientists, neither of whom are minority.

The race and grade level of the minority employees are provided below:

Position	Grade	Race
Health Scientist Administrator	GS-15	African-American
Scientific Review Administrator	GS-14	African-American
Scientific Review Administrator	GS-14	Asian
Personnel Management Specialist	GS-12	African-American
Grants Technical Assistant	GS-7	African-American
Grants Technical Assistant	GS-7	African-American
Administrative Assistant	GS-6	African-American
Secretary	GS-6	African-American
Secretary	GS-6	African-American
Secretary	GS-6	Indian
Secretary	GS-5	African-American
Clerk Typist	GS-5	African-American

In accordance with the NIH Federal Equal Opportunity Recruitment Program, we are actively recruiting minority individuals with graduate degrees in the area of nursing. To date, we have had limited success, primarily due to the relatively small number of such individuals available. We have however, achieved a marked increase in the numbers of minorities participating in our research training/career development programs. By providing minority supplements to institutional training grants, R01s, and P01s, we have been highly successful in increasing the cadre of qualified minority investigators with graduate degrees in nursing research. In fact, for the second year in a row, the NCNR has led the NIH with the highest number of minority supplements as a percentage of total eligible research grants.

MINORITY HEALTH RESEARCH

Mr. Stokes: Please describe for the committee the resources and funding levels which will be provided for minority-specific research activities in FY 1993. How do these levels compare to last year's levels? Total funding represents what percentage of your budget?

Dr. Hinshaw: Resources expended by the NCNR for research on minority health are expected to be $4.5 million under the FY 1993 President's Budget. In FY 1992, the level of funding is estimated to be $4.1 million. The percentage of NCNR total budget represented by research on minority health is 9.3 percent in FY 1993 and 9.1 percent in FY 1992.

Mr. Stokes: To what extent are you working with the Office of Minority Health to effectuate these goals?

Dr. Hinshaw: NCNR is working with the Office of Minority Health on the Adolescent Minority Health Initiative and the cooperative agreement to target infant mortality among blacks in Washington, DC. NCNR will continue to support research that targets the health care needs of minorities and will encourage additional efforts in high-priority areas such as community-based care of older people with chronic illness. Encouraging minority nurses to participate in research training is also a major priority for NCNR. Twenty-five minority nurses were supported in FY 1991. Continued efforts will be made to increase the numbers of nurses who seek training within the National Research Service Award program and through minority research supplements.

WOMEN'S HEALTH

Mr. Early: How do the common health problems of midlife women relate to the Women's Health Initiative?

Dr. Hinshaw: Very little is known about a diverse set of symptoms experienced by the majority of midlife women. Reports of weight gain, gastrointestinal problems, musculoskeletal pain, fatigue and sleep dysfunction, depression and vasomotor symptoms such as hot flashes are common and often the major reason for women to seek medical care, lose work time and experience a decrease in health related quality of life. These symptoms are often treated with medications with less than effective results.

The NIH Women's Health Initiative proposes to study the leading causes of mortality, morbidity, and declining quality of life in mature women in a three part study: by measuring the effectiveness of hormone replacement therapy, dietary modification and vitamin supplements to combat heart disease, cancer and osteoporosis; by seeking effective ways to promote healthy behavior within local communities; and by screening a large population of women for signs of progressive diseases and predictors of future illnesses.

By studying a large number of culturally and ethnically diverse midlife women over a period of time, information obtained in the NIH Women's Health Initiative will give scientists the opportunity to determine if any of these overlapping symptoms (or symptom combinations) are possible precursors or risk factors for the major chronic diseases of women. In addition the three different therapeutic trials will provide information on each of three individual interventions as well as interactions between interventions. This Initiative also provides an opportunity to obtain information on health promoting behaviors in women, as well as ethnic and cultural differences in health seeking and health promoting behaviors and responses to treatment.

Mr. Early: Doctor, what role will your institute play in the Women's Health Initiative? Would you give us a few examples of some of the research areas where NCNR will play a major role?

Dr. Hinshaw: NCNR staff have played a major role in the development of the Women's Health Initiative by participating in all of the working groups that designed the three part study, with special input in proposing a number of health quality of life measures. In addition, NCNR funded scientists have been identified and have served on Advisory Committees and Concept Review Panels for the Initiative.

Because no one study, no matter how large, can answer all of the myriad of questions related to women's health, NCNR will continue to support research that contributes to the overall goals of the NIH Initiative. Examples of currently funded related research include:

- Aiding midlife women to become more effective decision-makers regarding self-care and estrogen replacement therapy during menopause.

- Improving adherence to breast self-examination and mammography screening.
- Examining the impact of exercise training on overweight midlife women.
- Characterizing insomnia subtypes in midlife women and testing different sleep therapies.
- Studies on midlife health issues at a specialized Center for Women's Health Research.

REHABILITATION RESEARCH

Mr. Early: Doctor, your institute supports research in a number of areas which are also of interest to the National Center for Medical Rehabilitation Research. What type of working relationship have you established with the NCMRR? Do you have any collaborative efforts planned for FY 92 or FY 93?

Dr. Hinshaw: The NCNR works very closely with the National Center for Medical Rehabilitation Research (NCMRR). In fact, NCNR staff serve on the National Advisory Board for the NCMRR as well as NCMRR's Medical Rehabilitation Coordinating Committee. Collaborative efforts between the NCMRR and the NCNR are being explored in FY 1992 concerning a possible request for applications (RFA) on bowel and bladder management. In FY 1993, the NCNR and the NCMRR may be collaborating on two conferences--one related to pain and one related to integrated measurement systems.

MATERNAL AND CHILD HEALTH RESEARCH

Mr. Early: As you know, the Health Resources and Services Administration funds a number of programs related to maternal and child health, including the Infant Mortality Initiative and the MCH SPRANS Program. Is there any cooperation or coordination with the relevant Division of HRSA?

Dr. Hinshaw: NCNR is working collaboratively with several other PHS organizations on programs related to maternal and child health, including HRSA. We are co-funding a research project that is testing the effectiveness of nurse home visits to a high risk population of Black pregnant women and continue to collaborate with HRSA on projects that address rural health models of care to improve access to prenatal care services for minority populations.

HEALTH PROMOTION AND DISEASE PREVENTION

Mr. Early: Some of your Institute's research activities focus on preventive health and health promotion. To what extent do public health nurses participate in NCNR programs?

Dr. Hinshaw: Public Health Nurses have actively participated in both research and research training programs. Investigations have focused on testing models for promoting healthy behaviors in working adults, reducing cardiovascular risk factors in school age populations with specific nursing interventions, and testing nursing interventions to reduce high-risk behavior related to sexually transmitted diseases in clinic populations. Public Health Nurses continue to actively participate with the NCNR in establishing a national nursing research agenda for the future, as are other specialty groups interested in improving health care through nursing practice.

COLLABORATIVE RESEARCH

Mr. Early: Do you collaborate with CDC on areas of mutual interest? Would you give us some examples?

Dr. Hinshaw: The NCNR continues to look for opportunities to collaborate with other PHS agencies, such as CDC. In the past we have worked with CDC and NIA on an initiative to test interventions to prevent falls in frail older populations. We are collaborating with CDC on a study of accidental exposure of nurses in hospital settings to blood and other body fluids. We are beginning to collaborate with CDC as well on future initiatives that will address health promotion behaviors in adolescent populations.

ATTENTION DEFICIT DISORDERS

Mr. Early: Does your Institute support any research in the area of attention deficit disorders?

Dr. Hinshaw: Currently the NCNR is not funding research on attention deficit disorders, although there are longitudinal studies of low birthweight infants and their development that may identify such problems.

RESEARCH PROJECT GRANTS

Mr. Early: To what payline percentile will NCNR be able to fund under the budget request and how does this compare to the past two years?

Dr. Hinshaw: Under the FY 1993 President's Budget, the NCNR expects to fund to the 18th percentile. The percentile for FY 1992 is estimated to be 17, and in FY 1991, the percentile was 23.1.

CLINICAL TRIALS

Mr. Early: Are there any clinical trials that could be undertaken in FY 93 if additional resources were available?

Dr. Hinshaw: If additional resources were available, NCNR would conduct clinical trials to test several interventions that show promise with minority women in reducing the risk of delivering low birthweight infants. These interventions include culturally sensitive biological, behavioral, and social support components.

Mr. Early: Would you give us some examples of those approved but unfunded trials which you consider to be a high priority? And tell us why.

Dr. Hinshaw: NCNR has not solicited applications for clinical trials at this time.

Mr. Early: Please provide for the record a list of approved but unfunded clinical trials, along with a brief description of the trial, its duration, the first year cost and the estimated total cost of the trial.

Dr. Hinshaw: NCNR does not currently have a list of approved but unfunded clinical trials. We support a number of clinical intervention studies, but we are not presently involved with any large, NIH-defined clinical trials.

FINANCIAL MANAGEMENT PLAN

Mr. Early: What impact is limiting the average increase in the cost per award having on your research programs?

Dr. Hinshaw: In an effort to hold down the average costs of awarded grants, NCNR program officials and grants management staff are conducting prudent, pre-award negotiations of competing research project grant awards in compliance with the NIH Cost Management Plan. Beginning in FY 1991, NCNR instituted cost-containment policies that eliminate the arbitrary, across-the-board downward reductions which had been instituted in past years. Each competing grant is carefully examined to determine what level of budgetary adjustments can be implemented without adversely affecting the science of the proposed project.

In addition to cost analysis of proposed budgets, different grants, as well as separate categories of grants may be adjusted by different amounts based on program considerations and scientific relevance. This has enabled us to provide adequate funding to those scientific areas that are most promising. In implementing the principles of the NIH Cost Management Plan, we have been careful to ensure that the quality of research not be sacrificed in the interest of awarding low-cost grants. These funding measures have minimized the impact of limiting the average increase in the cost of nursing research grants.

STIPEND LEVELS

Mr. Early: What observations would you make about stipend levels as they pertain to your institute?

Dr. Hinshaw: Stipends for NRSA training grants awarded by NIH have not changed since FY 1991. Currently, stipend levels for predoctoral trainees supported by NIH are $8,800 per year. In comparison, the National Science Foundation pays $14,000, and the National Aeronautics and Space Administration pays $16,000. For postdoctoral trainees, stipends range from $18,600 to $32,300 depending on the number of years of post-doctoral experience the trainee possesses. The nursing community reports inadequate stipends given the current economic situation and the much higher salaries available for new nursing predoctoral graduates.

FULL-TIME EQUIVALENT POSITIONS

Mr. Early: The budget documents also reflect an increase, in FY 92 and FY 93, of the FTE's for both the intramural program and research management and support, tell us what your plans are in these areas.

Dr. Hinshaw: In FY 1992, NCNR's FTE levels for intramural research and research management and support are 9 and 39, respectively. FTE growth for the intramural research program has resulted from augmentation of preliminary research programs in symptom management of HIV infection. In FY 1993, additional positions are planned to support further investigations regarding health-related quality of life in individuals with HIV infection and the aging population.

In the research management and support activity, additional FTEs have been necessary to accommodate the rapid expansion of the Center's research programs and its growing grants portfolio, and to establish an adequate administrative infrastructure. The increase of two FTE's in FY 1993 will accommodate two additional nurse scientist administrators required in conjunction with the expansion of NCNR's extramural research initiatives in long-term care and women's health.

PROFESSIONAL JUDGMENT BUDGET

Mr. Early: What was the NCNR's professional judgment budget and how does it differ from the request before us?

Dr. Hinshaw: The FY 1993 Opportunities Budget for the NCNR totals $63,625,000, an amount approximately $15.1 million above the FY 1993 President's Budget. The major increases are described by mechanism below.

An additional $10 million was included for research project grants, allowing the NCNR to reach a success rate of 25 percent--a rate much closer to the NIH average of 26.4 percent. The increase also allows funding at the full level recommended by the Initial Review Group. Approximately $400,000 was included to establish three new exploratory centers focusing on long-term care and perinatal care. In the other research mechanism, approximately $1.2 million was included to initiate the Nurse Scientist Award program and provide funds for additional research career awards, as well as to initiate a small grants program focusing on biological studies. In research training, $2.2 million was included to provide funding for 320 research trainees, the level recommended by the National Academy of Sciences. A stipend increase was also included. An additional $700,000 was provided for the NCNR's newly established intramural research program. These funds would allow further expansion of studies focusing on health-related quality of life; specifically, symptom management of individuals with HIV infection and special care requirements of older adults. These funds would also allow the initiation of research protocols to study nursing care of cancer patients. The additional $300,000 provided for research management and support would allow for increases in centrally-furnished services as well as the implementation of a local area network (LAN).

FY 1993 PRESIDENT'S BUDGET

Mr. Early: Will any significant new research initiatives or opportunities be lost or delayed by lack of funds in the FY 93 budget request?

Dr. Hinshaw: In conjunction with the growth of nursing research as a scientific discipline, the number of high quality investigator initiated research project grant applications continues to increase each year. As in most areas of science, opportunities far outstrip available resources. This challenges us to set priorities and support the best proposals.

Carrying out the research priorities specifically set forth by the National Nursing Research Agenda (NNRA) will occur at a somewhat slower rate than envisioned, and more time will be required in disseminating information to the nursing community. The NNRA priorities are based on major public health issues such as low birthweight/infant mortality; HIV infection: prevention and care; long-term care for older adults; symptom management; nursing informatics; support for patient care; health promotion; and technology dependency across the lifespan. We will have to carefully balance the allocation of resources for Request for Applications (RFA's) and Program Announcements (PA's) in the NNRA program versus those for consolidated proposals. In some cases, there may be a delay in instituting the full agenda.

In the area of research training, the Center will support the same number of research trainees as in FY 1992. This reflects a conscious decision by NIH to place the highest priority on investigator-initiated research project grants, Women's Health, Minority Health (where significant training will occur) and the Intramural Research program.

Mr. Early: What priorities would the institute pursue if additional resources were available? If an increase over the FY 93 request is provided, how would you use these additional funds?

Dr. Hinshaw: If additional resources were provided over the FY 1993 President's Budget request, NCNR's first priority would be to increase the success rate for competing research project grants. This would be accomplished through earlier implementation of the planned initiative on acute pain in vulnerable populations, and additional awards under our long-term care and health promotion among midlife women initiatives.

Additional resources would also be used to expand NCNR's successful research centers program. Specifically, in addition to the on-going specialized centers focusing on women's health and acute illness, new specialized centers would be planned and established in the areas of long-term care and prevention of low birthweight.

NCNR's newly established intramural research program would also benefit from additional resources. This would enable expansion of studies focusing on health-related quality of life; specifically, symptom management of individuals with HIV infection and special care requirements of older adults, as well as the initiation of research protocols to study nursing care of cancer patients.

NATIONAL NURSING RESEARCH AGENDA

Mr. Pursell: What has NCNR accomplished from the National Nursing Research Agenda thus far? What are the next steps you will be taking with the NCNR priorities?

Dr. Hinshaw: The purpose of the National Nursing Research Agenda (NNRA) is to focus scientific endeavors and resources to build clusters of studies which are needed to improve practice for major public health problems. The agenda has been successful in accomplishing this objective. Stage I of the NNRA has been completed. As a result, clusters of studies are now being conducted in two areas of public health concern; i.e., prevention and care of low birthweight infants and mothers, as well as prevention of transmission of HIV infection and care of individuals with such infection. For example, the cluster of studies targeted to the prevention and care of low birthweight infants has grown from less than 5 to over 30 in a period of five years. The cluster of studies is particularly valuable in that interventions which are culturally sensitive to the prevention of low birthweight infancy are providing important information for working with vulnerable populations such as minority mothers. This set of studies has positioned the NCNR to have nursing actively involved in the Washington, DC, infant mortality project.

Stage II of the NNRA is currently being implemented. This provides for the focusing of resources in two major areas; i.e., 1) long term care of elderly people in the community and in nursing homes, with particular clinical conditions such as pressure sores, urinary incontinence, and confusion and 2) clinical assessment and management of acute pain. Stage II of the NNRA provides a window of opportunity for funding in these two important areas of study for 1992, 1993, and 1994. Stage III of the NNRA focusing on health promotion with children and adolescents and technology dependency across the lifespan will be implemented in 1994 and 1995. A conference with the nursing science and clinical practice community to update the priorities for the years 1995 to 2000 is planned for the late fall of 1992.

LONG-TERM CARE

Mr. Pursell: The number of older Americans continues to increase and many are chronically ill, what is NCNR doing to improve their health and functioning?

Dr. Hinshaw: IN FY 1992, NCNR will be funding over $6 million for research studies that target the long term care needs of older Americans. Studies include topics related to the control of incontinence, prevention of falls in frail older people, and nursing interventions to improve functioning after stroke. The NCNR long-term care program will be expanded in FY 1993 to target the development and testing of interventions for clinical problems occurring among older people in nursing homes, including problems related to mobility, cognition, and physical care, such as pressure sores, dehydration, and infections; depression; functional impairment; and social isolation. The goal of this expansion is to identify interventions that show promise in decreasing physical dependency and cognitive impairment;

preserving and improving functioning; facilitating self-care; increasing involvement of family members; and increasing the potential for discharge to home.

HEALTH PROMOTION AMONG CHILDREN AND ADOLESCENTS

Mr. Pursell: Why were children and adolescents selected as a priority population for health promotion studies in FY 1991?

Dr. Hinshaw: The NCNR targeted children and adolescents as the priority population for its health promotion program because the nation's dominant preventable health problems result from behaviors rooted in the emerging lifestyles of young people. Attitudes and habits related to diet, physical activity, alcohol abuse, tobacco use, and sexual behavior are formed early in life. Health-compromising habits established at this time not only impact on the immediate well-being of young people, but also may persist into adulthood, with major long-range implications for the onset of chronic disease.

FY 1993 PRESIDENT'S BUDGET

Mr. Pursell: We see that NCNR has an 8% increase in the President's Budget, the highest percentage increase at NIH. How did you manage to accomplish this?

Dr. Hinshaw: The NCNR did not have a direct role in determining the percentage increase allowed in the FY 1993 President's budget request. The nursing research community and NIH management should share the credit. There has been considerable interaction on this front, and NIH management has recognized the important role that nursing research will play in attaining the goals and objectives of the NIH strategic plan. The NCNR is very pleased with the support received from NIH. In an attempt to keep pace with the rapidly increasing numbers of investigator initiated research project grants that are being submitted to NCNR, and in an effort to recognize the importance of nursing research to the overall health of the American public, NIH management saw the value of providing NCNR with a slightly larger increase.

TRAVEL

Mr. Pursell: Given the travel restrictions passed earlier this year, what effect has this had on the nursing research programs at NCNR?

Dr. Hinshaw: The travel restrictions passed in FY 1992 have resulted in a ceiling reduction from $130,000 proposed in the Conference Allowance to the current ceiling of $62,000--a 52.3 percent reduction.

Mr. Pursell: We have heard that the travel restrictions have compromised the ability to carry out some of the research activities of the ICDs. What has been your experience at NCNR? Specifically, how have the FY 1992 travel reductions impacted on your ability to carry out your scientific mission?

Dr. Hinshaw: A 52.3 percent reduction in travel has had a severe impact on our programs. This is a particularly steep reduction for a small, but rapidly growing organization. To absorb this reduction, virtually all remaining travel has been canceled. The impact on our scientific mission has been considerable. For example:

- The September meeting of the National Advisory Council has been canceled. Applications received in response to two special requests for applications (RFAs) that must have Council approval before funding this fiscal year will have to be reviewed through a telephone conference call.

- No further site visits will be conducted. Funding decisions regarding applications received in response to special requests for applications (RFAs) will be made solely on the basis of Initial Review Group recommendations. Administrative or programmatic site visits to any of our existing grantees to assess progress or address administrative problems will not be possible.

- NCNR recently established an Intramural Research Program, with a number of research protocols being conducted in collaboration with the National Institute of Allergy and Infectious Diseases. Through this collaborative arrangement, we have been primarily working with patients who have been brought into the NIH for NIAID related studies. During FY 1992, however, the Intramural Program had planned to begin travelling its own patients in conjunction with studies which are focusing on the myopathy or muscle wasting developed by individuals during antiretroviral therapy for HIV infection. Because there were no patient travel funds included in our base from FY 1991, no funds were allowed under the reduced travel ceiling. As a result, NCNR will be unable to perform any patient travel in FY 1992.

- Since nursing research is a relatively new and rapidly growing discipline, there is a real need for information by nursing schools and others in the extramural research community concerning the mission of NCNR and how the NIH grant system works. There is a consistent demand for NCNR staff to travel into the community to conduct grantsmanship workshops and to be available to answer questions about the programs of the NCNR and NIH. Attendance at such workshops will not be possible under the reduced travel ceiling.

RESEARCH PROJECT GRANTS

Mr. Pursell: What would be NCNR's anticipated success rate for awards during FY 93 with the Administration's proposed budget for NCNR at $48 million?

Dr. Hinshaw: NCNR's estimated success rate for competing research project grants under the FY 1993 President's Budget is 15.5 percent.

Mr. Pursell: How many of those awards would be continuations and how many would be new?

Dr. Hinshaw: Under the FY 1993 President's Budget, the NCNR expects to fund 53 competing research project grants. Of these, it is estimated that 44 will be new competing awards and 9 will be competing continuations.

RESEARCH TRAINING

Mr. Pursell: What would be the number of research traineeships funded and how does the compare with FY 1992?

Dr. Hinshaw: In FY 1993, the budget request includes funds for 245 full-time training positions. This is the same number as in the FY 1992 appropriation. However, in FY 1991, 269 full-time training positions were supported.

SUCCESS RATES

Mr. Pursell: What is the NIH average success rate and how much funding would you need to bring NCNR's success rate up to that average?

Dr. Hinshaw: Under the FY 1993 President's Budget, the NIH average success rate for competing research project grants is estimated to be 26.4 percent. To increase NCNR's success rate from the current FY 1993 estimate of 15.5 percent to the NIH average of 26.4 percent would require an additional $7.7 million.

BENEFITS FOR SCHOOLS OF NURSING

Mr. Pursell: Aside from the money, what benefit do schools of nursing see in participating in NCNR's work? Have you or your students personally benefitted from NCNR, and if so, in what ways.

Dr. Hinshaw: Several faculty, students, and nursing investigators in service settings have stated that participation in the research enterprise has given them a different perspective on the health problems of patients and families that has a positive impact on their teaching and their practice. They also feel that colleagues in other disciplines have more respect for their ideas and contributions in the academic community as well as in service organizations. Collaboration with faculty from other schools is facilitated when others know that you have competed successfully within the NIH extramural programs.

Although there is always a significant amount of additional work involved, it is considered an honor to be asked to serve on review panels, on the National Advisory Council for Nursing Research, and on priority panels and tasks forces to provide recommendations to NCNR. It is recognition of an individual's expertise nationally and by colleagues in other disciplines that is helpful in advancing academic careers.

OUTCOMES FROM NURSING RESEARCH

Mr. Pursell: Can you give me some examples of improved nursing practice, cost effectiveness or outcomes resulting from nursing research funded by NCNR or otherwise?

Dr. Hinshaw: Several studies funded by NCNR are beginning to generate findings that can improve nursing practice and effect cost savings. One example is the study on confusion in hospitalized older persons that will allow for early and better interventions to prevent and treat confusion. Another study is finding ways to control nausea and vomiting as a result of chemotherapy for cancer treatment. Several studies are testing cost effective strategies to control incontinence in older persons, a major problem for many individuals living independently in the community as well as for people in nursing homes. New pain assessment tools also have promise for better detection and management of pain in children and in adults that may shorten recovery time. New strategies for discharge planning using expert nurses have also been validated as cost effective in several different populations.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Center for Nursing Research

FY 1993 Budget — Page No.

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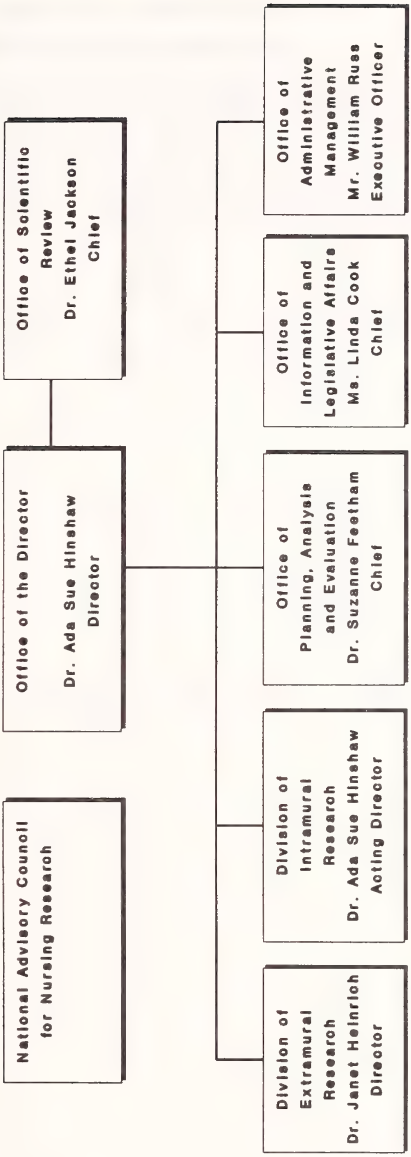
NATIONAL INSTITUTES OF HEALTH

National Center for Nursing Research

Organization Structure


National Advisory Council for Nursing Research
Office of the Director
Dr. Ada Sue Hinshaw
Director
Office of Scientific Review
Dr. Ethel Jackson
Chief
Division of Extramural Research
Dr. Janet Heinrich
Director
Division of Intramural Research
Dr. Ada Sue Hinshaw
Acting Director
Office of Planning, Analysis and Evaluation
Dr. Suzanne Feetham
Chief
Office of Information and Legislative Affairs
Ms. Linda Cook
Chief
Office of Administrative Management
Mr. William Russ
Executive Officer

NATIONAL INSTITUTES OF HEALTH

National Center for Nursing Research

For carrying out section 301 and title IV of the Public Health Service Act with respect to nursing research, [$45,196,000] $48,568,000: Provided, That of the funds made available under this heading [$2,646,000] $4,036,000 shall not become available for obligation until September 30, [1992] 1993.

(Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 1992.)

NATIONAL INSTITUTES OF HEALTH

NATIONAL CENTER FOR NURSING RESEARCH

Amounts Available for Obligation 1/

	1991 Actual	1992 Appropriation	1993 Estimate
Appropriation..................	$40,768,000	$45,196,000	$48,568,000
Sequester Order................	-1,000	---	---
Section 514(a) reduction.......	-64,000	---	---
Section 514(b) reduction.......	-982,000	---	---
Section 214 travel reduction...	---	-21,000	---
Section 513(a) travel reduction	---	-34,000	---
Section 513(b) S&E reduction...	---	-171,000	---
Subtotal, adjusted appropriation............	39,721,000	44,970,000	48,568,000
Real transfer from Other accounts for Shannon awards	+188,000	---	---
Subtotal, adjusted budget authority........	39,909,000	44,970,000	48,568,000
Unobligated balance, lapsing....................	-17,000	---	---
Total, obligations........	39,892,000	44,970,000	48,568,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1991 - $2,807,000; 1992 - $4,270,000; 1993 - $4,270,000.

NATIONAL INSTITUTES OF HEALTH

National Center for Nursing Research

Budget Mechanism

(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	No.	Amount	No.	Amount	No.	Amount
Research Grants:						
Research projects						
Noncompeting..............	111	$18,659	118	$22,962	118	$24,093
Admin. supplemental.......	(7)	107	(6)	308	(6)	319
Competing						
Renewal.................	9	2,076	7	1,697	9	2,247
New.....................	40	6,888	36	6,658	43	8,313
Supplemental............	1	74	1	150	1	158
Subtotal, competing.....	50	9,038	44	8,505	53	10,718
Subtotal, res. proj.........	161	27,804	162	31,775	171	35,130
Research Centers...........	7	1,630	7	1,639	7	1,639
Other Research						
Research career program...	12	885	12	1,041	12	1,041
Other research related....	18	1,046	14	1,031	14	1,031
Subtotal, other research	30	1,931	26	2,072	26	2,072
Total, research grants........	198	31,365	195	35,486	204	38,841

Training:						
Individual awards:						
Noncompeting	100	1,234	110	1,388	100	1,460
Competing						
New	62	802	39	666	48	671
Renewal	0	0	4	68	5	69
Subtotal, individual	162	2,036	153	2,122	153	2,122
Institutional awards:						
Noncompeting	107	2,300	59	1,288	80	2,072
Competing						
New	0	0	23	684	8	245
Renewal	0	0	10	298	4	125
Subtotal, Institutional	107	2,300	92	2,270	92	2,270
Total, training	269	4,336	245	4,392	245	4,392
Research and development contracts	1	100	2	150	2	150
Intramural research	FTE (5)	550	FTE (9)	773	FTE (10)	812
Research management and support	(33)	3,558	(39)	4,169	(41)	4,373
Total	(38)	39,909	(48)	44,970	(51)	48,568

NATIONAL INSTITUTES OF HEALTH

National Center for Nursing Research

CROSSWALK - 1991 Actual
(Dollars in thousands)

	MECHANISM								
	Research Grants			Training Programs					
PROGRAM ACTIVITY	Research Projects	Research Centers	Other Research	Individual	Institutional	Research & Development Contracts	Intramural Research	Research Management & Support	Total
Nursing Research...	$27,804	$1,630	$1,931	$2,036	$2,300	$100	---	---	$35,801
Intramural Research	---	---	---	---	---	---	$550	---	550
Research management and support......	---	---	---	---	---	---	---	$3,558	3,558
Total.......	27,804	1,630	1,931	2,036	2,300	100	550	3,558	39,909

NATIONAL INSTITUTES OF HEALTH

National Center for Nursing Research

CROSSWALK - 1992 Appropriation
(Dollars in thousands)

	MECHANISM								
	Research Grants			Training Programs					
PROGRAM ACTIVITY	Research Projects	Research Centers	Other Research	Individual	Institutional	Research & Development Contracts	Intramural Research	Research Management & Support	Total
Nursing research..	$31,775	$1,639	$2,072	$2,122	$2,270	$150	---	---	$40,028
Intramural research	---	---	---	---	---	---	$773	---	773
Research management and support.....	---	---	---	---	---	---	---	$4,169	4,169
Total.......	31,775	1,639	2,072	2,122	2,270	150	773	4,169	44,970

NATIONAL INSTITUTES OF HEALTH
National Center for Nursing Research

CROSSWALK - 1993 Estimate
(Dollars in thousands)

PROGRAM ACTIVITY	MECHANISM								
	Research Grants			Training Programs					
	Research Projects	Research Centers	Other Research	Individual	Institutional	Research & Development Contracts	Intramural Research	Research Management & Support	Total
Nursing Research...	$35,130	$1,639	$2,072	$2,122	$2,270	$150	---	---	$43,383
Intramural Research	---	---	---	---	---	---	$812	---	812
Research management and support......	---	---	---	---	---	---	---	$4,373	4,373
Total.........	35,130	1,639	2,072	2,122	2,270	150	812	4,373	48,568

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NATIONAL INSTITUTES OF HEALTH

National Center for Nursing Research

Summary of Changes

1992 Estimated budget authority	$44,970,000
1993 Estimated budget authority	48,568,000
Net change	+ 3,598,000

	1992 Current Estimate Base		Change from base	
Increases:	Pos. (FTEs)	Budget Authority	Pos. (FTEs)	Budget Authority
A. Built-in:				
1. Within-grade increases		$2,630,000		+$28,000
2. Annualization of 1992 payraise		2,630,000		+30,000
3. One less day of pay			--	-10,000
4. Cost of 1993 payraise		2,630,000		+88,000
5. Payment for centrally furnished services		884,000		+112,000
6. Service and supply fund increase		165,000		+8,000
7. Increased cost of laboratory materials and other supplies		1,211,000		+45,000
8. DHHS Working Capital Fund		52,000		+3,000
Subtotal				+304,000
B. Program:	No.	Amount	No.	Amount
1. Research projects grants:				
a. Noncompeting	118	$23,270,000		+$1,142,000
b. Competing	44	8,505,000	+9	+2,213,000
Total	162	31,775,000	+9	+3,355,000
	FTEs		FTEs	
2. Intramural research	9	773,000	+1	-37,000
3. Research management and support	39	4,169,000	+2	-24,000
Subtotal				+3,294,000
Total changes			+3	+3,598,000

NATIONAL INSTITUTES OF HEALTH

National Center for Nursing Research

Budget Authority by Activity
(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	FTE	Amount	FTE	Amount	FTE	Amount
Nursing research	---	$35,801	---	$40,028	---	$43,383
Intramural research	5	550	9	773	10	812
Research management and support	33	3,541	39	4,169	41	4,373
Subtotal, obligations		39,892		44,970		48,568
Unobligated balance lapsing		17		---		---
Total budget authority	37	39,909	48	44,970	51	48,568
HIV/AIDS	(5)	(2,545)	(7)	(3,193)	(8)	(3,337)

NATIONAL INSTITUTES OF HEALTH

National Center for Nursing Research

Budget Authority by Object

	1992 Appropriation	1993 Estimate	Increase or Decrease
Total number of full-time permanent positions................	50	52	+2
Total compensable workyears:			
Full-time equivalent employment....	49	52	+3
Full-time equivalent of overtime and holiday hours................	1	1	0
Average ES salary....................	$102,012	$105,786	+$3,774
Average GM/GS grade..................	10.7	10.7	0
Average GM/GS salary.................	43,311	45,606	+2,295
Average salary, grades established by act of July 1, 1944 (42 U.S.C. 207)	52,048	53,974	1,926
Personnel compensation:			
Full-time permanent.................	$1,579,000	$1,737,000	+$158,000
Other than full-time permanent.......	231,000	252,000	+21,000
Other personnel compensation.........	360,000	392,000	+32,000
Subtotal, personnel compensation	2,170,000	2,381,000	+211,000
Personnel benefits...................	460,000	502,000	+42,000
Travel and transportation of persons.	62,000	95,000	+33,000
Transportation of things.............	13,000	13,000	---

	1992 Appropriation	1993 Estimate	Increase or Decrease
Rent, communications and utilities	75,000	75,000	---
Printing and reproduction........	70,000	70,000	---
Other services:			
Project contracts.............	150,000	150,000	---
Centrally furnished services...	884,000	1,031,000	+147,000
Other........................	1,021,000	831,000	-190,000
Supplies and materials...........	77,000	77,000	---
Equipment.......................	110,000	110,000	---
Grants, subsidies and contributions..................	39,878,000	43,233,000	+3,355,000
Total budget authority by object...................	44,970,000	48,568,000	+3,598,000

NATIONAL INSTITUTES OF HEALTH

National Center for Nursing Research

Significant Items in Senate and Conference Appropriations Committee Reports

Health Promotion Among Children and Adolescents

The Senate in its report 102-104, p. 137, stated "The Committee urges continued priority be given to health promotion among children and adolescents. Of the 10 leading causes of death in the United States, each is in part behaviorally determined. Children and adolescents within our society are of special concern, because this period of life is critical in the development of health compromising and health promoting behaviors. To address this problem, the NCNR established an exploratory research center to investigate health behavior development in children and adolescents. This new center, along with other ongoing projects will focus on development and testing of health-enhancing models of behavior. The basic knowledge gained from these studies will lay the foundation for the primary prevention of disease and the promotion and maintenance of healthy lifestyles across the lifespan."

Action Taken or to be Taken - The NCNR has initiated a research program concerning health promotion among children and adolescents that will focus on dominant preventable health problems in emerging lifestyles. Particular emphasis will be placed on children of traditionally underserved populations, i.e., racial and ethnic minorities and those of lower socioeconomic status. The NCNR is currently funding three exploratory centers focusing on health promotion among children and adolescents. Studies at one center will focus on the cognitive factors underlying the initiation and maintenance of health promoting and risk-taking behaviors; another center will focus on the health behaviors of Mexican-American and African-American adolescents; and the third center will focus on health promotion among rural youth. Examples of other research currently supported by NCNR in the area of health promotion among children and adolescents include a longitudinal investigation of physiologic, behavioral and life-style risk factors for cardiovascular disease in twin children and their parents and a study to identify cardiovascular risk factors among rural and urban children and test the effectiveness of different cardiovascular disease risk-factor interventions.

Rural Health Care

The Senate in its report 102-104, p. 138, stated "Funding is provided to address the special health care needs of individuals residing in rural areas. Specifically, the health status of individuals, their health-care requirements, and the most effective methods of delivering health care to them are being addressed. The Committee is pleased that the NCNR has expanded this initiative to vulnerable populations, particularly those at risk for chronic illness and disabilities, and those requiring increased primary care to achieve wellness."

Action Taken or to be Taken - The special health care needs of individuals residing in rural areas is the focus of an NCNR special initiative. Specifically, the health status of individuals, their health-care requirements, and the most effective methods of delivering health care to them are being addressed. NCNR's research portfolio in this area includes two research demonstration projects on community-based rural health care that are testing innovative nursing interventions for minority populations. Other projects are focusing on health care needs of the chronically ill elderly and issues surrounding care for pregnant women, including access to prenatal care. Furthermore, one of the new exploratory centers on adolescent health and behavior recently funded by NCNR will focus on rural youth. In particular, one investigator will examine the factors involved in the initiation and maintenance of tobacco use among rural teens.

Additionally, the NCNR recently convened the first meeting of the Rural Health Research Advisory Committee. This group consisted of scientists, nurse clinicians, and other rural health experts. These experts were asked to assist NCNR by defining issues in rural health care and research, identifying strategies for meeting the needs of clinicians and investigators involved in rural health, and to make recommendations for future activities. Areas of clinical concern that the group stressed were behavioral health problems, such as smokeless tobacco and alcohol abuse, mental health problems, such as depression, and occupational hazards, such as farm injuries and trauma to children working on family farms.

NCNR staff have also provided workshops and other consultation to rural health investigators in North Dakota, West Virginia, Wisconsin, and at a national rural health meeting in Washington state.

Vulnerable Populations

The Senate in its report 102-104, p. 138, stated "The Committee is pleased that progress has been made in encouraging research that targets the health care concerns of rural Americans, especially vulnerable populations such as Native Hawaiians, minority pregnant women and their infants. The Committee was very pleased to recently learn that the NCNR has established a special Native American nursing task force in order to ensure that continued attention is given to their truly pressing health care needs."

Action Taken or to be Taken - Initial contacts with Native Indian/Alaska Native nurses, many of whom work within the Indian Health Service (IHS), PHS, have been made. The Director, NCNR, spoke at an IHS research development conference in New Mexico in the Fall of 1991 and assisted Native American nurses in the development of plans for research training and the identification of resources for addressing major Native American health problems. NCNR participated in a meeting hosted by the American Nurses Association and the IHS Division of Nursing to discuss the needs of nurses in addressing health care needs of Native Americans. A future meeting is planned in conjunction with nurse leaders in the IHS. Native American nurses will also participate with the NCNR Ad Hoc Task Force on Minority Health.

HIV Infection

The Senate in its report 102-104, p. 138, stated "The Committee is pleased that NCNR is funding several projects focusing on the prevention and care of HIV infection. Topics include the physiological and psychological factors in HIV-positive individuals and their caretakers, optimum modalities of nursing care for hospitalized patients; evaluation of patient care needs during the course of practicing high-risk behaviors. The efforts to work with other agencies in encouraging international behavioral research in support of AIDS prevention are to be particularly applauded . . . The Committee is encouraged to learn that new studies will measure health-related quality of life, using subjects participating in ongoing clinical trials. The Committee further recommends that NCNR make special effort to involve other disciplines, such as psychology, in these research endeavors."

Action Taken or to be Taken - Research on HIV infection has been designated as an NCNR priority in the National Nursing Research Agenda. Areas of concern include prevention of transmission, psychological aspects of nursing care, psychosocial aspects of nursing care, delivery of nursing care, and support for caregivers. NCNR currently supports studies on the nursing care needs of patients and their families at different stages of disease with a focus on symptoms. The objectives of these studies are to determine quality-of-life measures and characterize the progression of the disease. The conduct of these HIV/AIDS clinical studies will lead to effective interventions that will maintain optimal functioning of infected individuals and their families.

Nurse Training

The Conference in its report 102-282, 29, stated "The conferees believe a concerted effort should be made to enhance the quantitative analysis skills of nursing faculty during the coming year.

Action Taken or to be Taken - Nursing research programs are rapidly developing in many institutions. A strong cadre of trained nurse investigators is needed to address the complex problems related to improved patient care. A summer methodology institute is planned that will address linkages between behavioral and biological quantitative measures as well as state-of-the-art methodologies in clinical research. Participants will include faculty from schools of nursing and experts in human behavior and health from other disciplines.

NATIONAL INSTITUTES OF HEALTH

National Center for Nursing Research

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1992 Amt. Authorized	1992 Appropriation	1993 Amt. Authorized	1993 Budget Request
Research and Investigation..	Section 301	42§281	Indefinite	$40,578,000	Indefinite	$44,176,000
National Center for Nursing Research..................	Title IV, Part E	42§287	Indefinite		Indefinite	
National Research Service Awards....................	Section 487(d)	42§288	Authorizing 1/ legislation is pending	4,392,000	Authorizing 1/ legislation is pending	4,392,000
Total Budget Authority...				44,970,000		48,568,000

1/ This training authority is shared with other research training programs of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration.

NATIONAL INSTITUTES OF HEALTH

National Center for Nursing Research

Appropriation History 1/

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1987	---	$16,700,000	$20,000,000	$20,000,000
1988	$16,133,000	24,744,000 2/	23,566,000	23,380,000
1989	24,400,000 3/	27,417,000 4/	28,107,000	29,139,000
1990	29,970,000 5/	32,969,000	34,969,000	33,935,000 6/
1990 Sequester				-422,000
1991	35,127,000	37,289,000 7/	40,013,000	39,722,000 8/
1991 Sequester				-1,000
1992	43,747,000	43,143,000	45,880,000	44,970,000 9/
1993	48,568,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.

2/ Does not include funding for AIDS research consolidated at the Secretary's level.

3/ The 1989 request excludes funds for AIDS research and education ($707,000) proposed for consolidation in the Office of the Assistant Secretary for Health.

4/ Excludes $2,690,000 in NRSA training programs not considered.

5/ The 1990 request excludes funds for the National HIV Program ($999,000) proposed for consolidation in the Office of the Assistant Secretary for Health.

6/ Exlcudes enacted administrative reduction of $34,000.

7/ Exludes $4,233,000 in NRSA training programs not considered.

8/ Excludes enacted administrative reductions of $1,046,000.

9/ Excludes enacted administrative reductions of $226,000.

Justification

National Center for Nursing Research

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
38	$39,893,000	48	$44,970,000	51	$48,568,000	+3	+$3,598,000

General Statement

The National Center for Nursing Research (NCNR) was established to build a strong scientific base for nursing practice. NCNR research reflects the diverse caregiving responsibilities of nurses in every segment of society from meeting the specialized care needs of low birthweight infants to helping heart attack patients regain normal functioning. Research is helping nurses in the community provide optimum assistance to individuals coping with chronic illness, to family caregivers, to low income families, and to older persons struggling to maintain their independence.

NCNR supports studies on innovative approaches to promoting health and preventing disease, minimizing the effects of acute and chronic illness and disability, and speeding recovery from diseases. NCNR-supported studies are also concerned with improving the systems and settings for nursing care and examining the ethics of clinical decision making.

The research efforts of the NCNR encompass both extramural and intramural programs. The three branches comprising the extramural program are the Acute and Chronic Illness Branch, the Health Promotion and Disease Prevention Branch, and the Nursing Systems Branch. The Acute and Chronic Illness program supports research on patient and family responses to acute and chronic illness and disability, on the biological and behavioral factors that contribute to these conditions, and on ways to improve or remedy them. It includes aspects of nursing care related to AIDS, chronic dialysis, diabetes management, wound healing and recovery from surgery. Health promotion research focuses on improving general health and quality of life. It concerns such issues as pregnancy health behavior, adolescent health habits, dieting practices, smoking and health behavior, and bereavement. Disease prevention research addresses early detection and treatment of particular disease or conditions, such as hypertension, cardiovascular disease, cancer, or loss of bone mineral density. The Nursing Systems program funds studies on new approaches to quality nursing services, and management strategies to improve patient care. It is concerned with innovative nursing care delivery models, as well as such issues as decision making in critical care settings, nurse midwifery and patient outcomes, and endpoints of home care nursing. Bioethics research, particularly clinical decisions made by patients, families, and providers, is a special initiative of the Nursing Systems program.

The Division of Intramural Research develops and conducts basic and clinical research that contributes scientific knowledge pertinent to nursing practice and health care of individuals. Current studies focus on symptom management of people with HIV infection, compliance with treatments of HIV infection, and quality of life related to Alzheimer's disease. The Intramural Research Program also provides training opportunities for nurse scientists.

During the past fiscal year research funded by the NCNR has led to scientific advances in the areas of infant health and mortality, behavioral research, and chronic and recurrent diseases and rehabilitation.

Infant Health and Mortality. Advances in our understanding of the neurological development of low birthweight infants have increased our ability to identify infants who require special handling. One investigator has been collecting data concerning the sucking behaviors of full-term and pre-term infants. Abnormal sucking patterns were documented in one-third of the known cocaine-exposed infants who had not previously been suspected of being behaviorally impaired. This finding indicates that the assessment of sucking behaviors is a sensitive method of evaluating neurological development in such infants.

Behavioral Research. Progress has been made in stretching limited mental health resources to help the families of conduct-problem children who may be at risk for future antisocial behavior. Videotaped modeling is an effective means of parent training. A team of investigators has now demonstrated that a self-administered videotaped program results in significant improvements in parenting skills and significant reductions in child behavior problems. Furthermore, the videotaped program offers the parents privacy, flexible scheduling, self-pacing, and self-control. This program's cost-effectiveness and potential to be easily disseminated to large numbers of people make it an appealing alternative to the more traditional forms of treatment for child behavior problems.

Chronic and Recurrent Diseases and Rehabilitation. A home-based program is being developed to help individuals with Alzheimer's disease (AD) and their families. This program addresses AD patients' difficulties with conversation, memory, and problem-solving through mental stimulation exercises administered by family caretakers for 1 hour each day. Initial results are very promising for both patients and caretakers. Patients who participated actively in the practice sessions showed improved mental functioning during the treatment period, while those in the nontreatment (control) group showed a continuing decline. Behavioral problems, which are often a significant factor in the management of AD patients, tended to remain stable in the treatment group, but to increase markedly in the nontreatment group. The intervention also helped family caretakers, who reported a decline in physical symptoms. In addition to improving the health and well-being of Alzheimer patients and their caretakers, this innovative program can potentially reduce the financial burden of AD by extending the time patients can avoid costly institutionalization and remain at home with their families.

New program initiatives or enhancements planned for the future include biobehavioral interventions to deal with neurological symptomology, women's health research focusing on normal processes in midlife, and long-term care of frail older people.

Symptom management for patients with neurological disorders. The human responses to neurological disorders frequently include symptoms that present major health care management problems. Effective interventions are needed to deal with neurological symptoms resulting from conditions such as stroke, brain or spinal cord injury, or neurological damage from toxic treatments. NCNR is currently supporting investigations of stroke patients in addition to studies dealing with the management of confusion resulting from environmental, physiological, and toxic factors; spatial disturbances and disorientation symptoms associated with brain damage; and cognitive impairment resulting from whole brain radiation and intrathecal chemotherapy. For example, this new initiative will advance research to detect early signs of impending confusion in hospitalized elderly patients. Additional study is needed for the identification of factors, such as cognitive status, oxygenation status, and renal function, which provide intervention opportunities to effectively manage the three types of documented confusion--environmental, physiological, and toxic. This initiative also builds on research which is testing an animal model of human disorientation to understand the basic neural and cognitive mechanisms associated with the ability to acquire and use spatial information in varying environmental cue situations. Additional study is also needed for the current research with children being treated for acute lymphoblastic leukemia, brain tumors, and disorders requiring bone marrow transplants in order to identify those at risk for cognitive impairment from the treatments. Neurochemical measurements and techniques are being used to determine the relationship of radiation dose, chemotherapy levels, and CNS damage/cognitive impairment.

Women's health research focusing on normal processes in midlife. Midlife women account for a growing proportion of the U.S. population; currently there are 40 million midlife women with a life expectancy of 28 years following menopause. A few studies on midlife women have focused narrowly and predominantly on menopausal symptoms; little is know about health patterns, their general health, and the steps they take to promote and maintain their health. Highly prevalent in women in midlife are syndromes involving musculoskeletal symptoms, gastrointestinal symptoms, fatigue, and vasomotor instability. Common features include no clear pathology, extensive symptom overlap, and concurrent high levels of psychological distress. This symptom complex is a major reason for seeking medical care, disability, and lost work time. Investigation is needed on the role of reproductive hormone transitions in contributing to and/or accentuating these symptoms, and the role of reactivity/stress responsivity in understanding these phenomena in midlife women. An understanding of cultural influences, and ethnic comparisons are also critical components of these studies. The ultimate goal of this initiative is to decrease the excess morbidity experienced by midlife women that carries over into their later years, and to significantly increase the quality of life experienced by midlife and ultimately aging women as they live out their longer life spans.

Clinical care problems for older persons in nursing homes. The NCNR will expand the research program in long-term care requirements of older persons to include an initiative to investigate clinical care strategies for residents of nursing homes. This initiative will build on the recommendations of a panel of scientists who are developing the long-term care component of the National Nursing Research Agenda. The emphasis on clinical care in nursing homes will complement the existing research emphasis of the program on community-based clinical interventions for older persons with chronic illnesses. More specifically, the planned program expansion will include studies on balance and gait that will lead to interventions to prevent falls. Related areas include mobility and range of motion studies that recognize the heterogeneous abilities of older persons in nursing homes. The purpose of the initiative is to develop and test clinical interventions that show promise in preserving, rehabilitating, and improving functioning; decreasing dependency; increasing quality of life and care; and improving clinical outcomes. Studies will address the need among nursing home residents for intervention strategies that provide individualized care, participation in self care, increase in functional status and independence, increased involvement of family members, and that recognize the potential for rehabilitation and discharge to home. Previous studies have focused on administrative aspects of nursing home care or have limited their investigations to comparisons with non-nursing home residents. This new initiative will provide the opportunity to investigate the unique clinical environments of nursing homes and test interventions that build on current clinical research.

Funding for the National Center for Nursing Research during the last 5 years has been as follows:

	Amount	FTE
FY 1988	$23,380,000	25
FY 1989	29,139,000	31
FY 1990	33,513,000	28
FY 1991	39,909,000	38
FY 1992	44,970,000	48

Purpose and Method of Operation

Extramural research and training are supported through the Nursing Research budget activity, which is comprised of three program areas: Acute and Chronic Illness, Health Promotion and Disease Prevention, and Nursing Systems. Funding mechanisms include research project grants, research centers, other research grants, research training, and research and development contracts. Intramural research is conducted through the Clinical Therapeutics Laboratory, and the Laboratory for the Study of Human Responses to Health and Illness. The leadership and scientific direction of the Institute are funded through the Research Management and Support activity.

Overall Budget Policy

The FY 1993 budget request for the NCNR totals $48,568,000, including $3,337,000 for AIDS research. This amount represents a total increase of $3,598,000 or 8 percent over FY 1992.

The FY 1993 budget request for research project grants is $35,130,000. This level will support 118 noncompeting research project grants, at an average cost of $204,000, and 53 competing research project grants, at an average cost of $202,000; resulting in an overall average cost increase of 4.7 percent and 9 awards over 1992.

In research centers, the request provides $1,639,000 to continue funding seven centers. This is the same amount provided in FY 1992.

The FY 1993 request provides the same amounts in the other research mechanism as in FY 1992. This allows funding for 12 research career awards, approximately 12 small grant and instrumentation grants, and continued support for two research demonstration projects.

In research training, the amount provided is $4,392,000, which will allow funding for 245 full-time training positions, the same as provided in FY 1992.

The amount requested for research and development contracts is $150,000, the same level as FY 1992.

The FY 1993 request provides $812,000 for intramural research, an increase of $39,000. This amount will cover cost increases for centrally furnished services, laboratory supplies and services, and salaries.

In research management and support, the FY 1993 request provides $4,373,000, an increase of $204,000 over FY 1992. Included in this amount are built-in administrative cost increases. This level will support 41 FTEs.

National Center for Nursing Research

Nursing Research

Authorizing Legislation - Section 301 and 483-486, 487 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$35,801,000	$40,028,000	$43,383,000	+$3,355,000

This activity supports research, research training, and career development awards in the following three major program areas:

Acute and Chronic Illness: This program supports research on the human responses to acute and chronic illness and disability, on the biological and behavioral factors that contribute to these conditions, and on ways to improve or remedy these conditions. Some examples of supported studies are: coping with dyspnea in asthma; nursing care of persons with AIDS; family management of intravenous therapy in children in home care; altered immune responses in chronic dialysis patients; conditions affecting success with diabetes management; nursing assessment of pressure sore risk; and social support/well-being of chronically ill elderly.

Health Promotion/Disease Prevention: Health promotion research focuses on nursing approaches to improving general health and health care. This includes ways to promote wellness and to decrease the vulnerability of individuals and families to illness and disability. Currently funded health promotion research projects include: factors in pregnancy health behavior and outcomes; health compromising behaviors among young adolescents; nursing concerns regarding characteristics of successful dieters; factors influencing health promoting behaviors; smoking and health behavior; factors affecting bereavement; nursing care of older persons; and interventions to promote health in older persons. Disease prevention research addresses particular diseases or disabilities. Funded projects include: community-based education program for black hypertensives; reducing cardiovascular risk; physical activity patterns and bone mineral density; and breast self-examination.

Nursing Systems: This program addresses the environmental influences affecting the delivery of nursing care. Of particular interest are studies on innovative approaches to the delivery of quality nursing services, management strategies to improve patient outcomes, and interventions to assure the availability of nursing resources. Bioethics research which focuses on clinical practice, particularly clinical decision making, is a special initiative of the Nursing Systems program. Currently funded topics are: innovative nursing care delivery models for improving patient care and fostering nurse retention; diverse effects on patients of hospital noise control; nursing resource use in home care; the influence of high stress clinical practice settings on nurse retention; evaluation of home care for cancer patients; and the influence of nurse midwifery practice on patient outcomes.

Funding for the Nursing Research budget activity during the last 5 years has been as follows:

	Amount
FY 1988	$21,344,000
FY 1989	26,681,000
FY 1990	30,462,000
FY 1991	35,801,000
FY 1992	40,028,000

Rationale for the Budget Request

The FY 1993 budget request for the Nursing Research budget activity is $43,383,000, an increase of 8.4% over the FY 1992 estimate of $40,028,000. The following are examples of research activities funded in this program.

Long-term Care Requirements of Older Persons

The community-based care for chronically ill older persons initiative builds directly on the work of a panel of scientific experts on long-term care convened as part of the development of the National Nursing Research Agenda. The goal of the initiative is to stimulate the development of innovative clinical interventions for community-based, chronically ill older people in order to manage commonly experienced symptoms, prevent the onset of further disabilities, and facilitate the transition between health care settings and home. The outcomes would be expected to encourage independence, enhance health-related quality of life, and enable the chronically ill older person to remain at home.

Community-based long-term care represents a continuum of care during which older people with chronic illnesses make transitions through several health care settings with the continuing emphasis on home care. The concern of this initiative is to support research that will assist in building a foundation of knowledge that will facilitate older people with chronic illness to remain living at home among their family. NCNR is currently supporting studies that examine ways to improve the transition between hospital and home care for patients with cancer and to determine the effectiveness of a cognitive stimulation protocol taught to family members and implemented with patients with Alzheimer's Disease.

Symptom Management: Acute Pain in Vulnerable Populations

In the development of the National Nursing Research Agenda (NNRA), the NCNR designated symptom management as a priority area for the development of knowledge for nursing practice. Subsequently, the NNRA expert panel on symptom management identified pain as one of four symptoms to receive special attention. The initial focus of this priority area will be on the assessment and management of acute pain and exacerbations of acute pain associated with chronic illness, particularly as it relates to vulnerable populations such as children, minorities, the cognitively impaired, and older persons.

Caring for patients in pain is an extremely complex issue due to the multidimensional nature of pain, including physiological, sensory, affective, cognitive, behavioral, and sociocultural attributes. Patient care is further complicated by the difficulty of accurate pain assessment and treatments that are often inadequate for effective pain relief. These problems are compounded in vulnerable populations who may have problems understanding, expressing, and coping with pain. This initiative will address the special pain assessment and management issues in these individuals. For the purpose of this research program, acute pain will include pain due to cancer as well as episodes of acute pain associated with chronic illness, such as sickle cell disease and rheumatoid arthritis. The overall goal will be to improve pain assessment techniques and to identify integrated multimodal treatments including pharmacological and nonpharmacological approaches to pain management.

Health Promotion Among Children and Adolescents

The NCNR has initiated a research program concerning health promotion among children and adolescents that will focus on dominant preventable health problems in emerging lifestyles. Attitudes and habits related to diet, physical activity, alcohol abuse, tobacco use, and sexual behavior may persist from adolescence into adulthood, compromising health in the short term and having major long-range implications for the onset of chronic disease. These initiatives have focused on development and testing of health-enhancing models of behavior. The basic knowledge gained from these studies will lay the foundation for the primary prevention of disease and the promotion and maintenance of healthy lifestyles across the lifespan.

Particular emphasis will be placed on children of traditionally underserved populations, i.e., racial and ethnic minorities and those of lower socioeconomic status. Because the family is the context within which many children learn health behaviors, determining factors that strengthen the role of the family in establishing health-promoting behaviors is an area that will be studied.

In FY 1991 the NCNR co-sponsored a request for applications with the National Institute of Child Health and Human Development and the National Institute of Mental Health to establish multi-disciplinary exploratory Centers for Adolescent Health Promotion. The NCNR is currently funding three centers.

Studies at one center will focus on the cognitive factors underlying the initiation and maintenance of health promoting and risk-taking behaviors. One pilot study will examine the effects of school transition on alcohol use and misuse in adolescents. Another team of investigators will look at the antecedents, patterns and health outcomes of exercise among adolescents. The cognitions of self as related to health behaviors will be examined in a racially and economically diverse sample in a third study. An additional group will look at the antecedents of negative health behavior among teenagers.

Another center will focus on the health behaviors of Mexican-American and African-American adolescents. In one pilot study, a nursing intervention designed to promote healthy behaviors among pregnant teens will be tested, A second study will examine the perceptions of body weight, nutrition and exercise among Hispanic adolescents and test an "upbeat, fun" nutritional educational intervention. A third group of investigators will test two interventions designed to improve oral health promotion among Mexican-American tenth graders.

At the third center, the focus of the adolescent health promotion will be rural youth. One investigator will examine the factors involved in the initiation and maintenance of tobacco use among rural teens. A second project looks at children's attitudes, intentions, and expectancies toward demographic factors, diet and health behavior on zinc deficiency among pregnant adolescents and subsequent infant outcomes.

Examples of other research currently supported by NCNR in the area of health promotion among children and adolescents include a longitudinal investigation of physiologic, behavioral and life-style risk factors for cardiovascular disease in twin children and their parents and a study to identify cardiovascular risk factors among rural and urban children and test the effectiveness of different cardiovascular disease risk-factor interventions.

Low Birthweight: Prevention and Neonatal Nursing Care

In spite of considerable national attention during recent years, the infant mortality rate in the United States remains unacceptably high. Low birthweight (LBW) accounts for nearly two-thirds of the more than 45,000 infants who die each year in the United States. The disparity in low birthweight rates among populations subgroups is persistent, with black women living below the poverty line particularly at risk for delivering LBW infants. NCNR, in collaboration with NICHD, is encouraging interdisciplinary teams of basic and clinical scientists to address issues related to caring for low birthweight babies as well as issues related to the prevention of LBW.

The neonatal intensive care unit (NICU) is an important factor in the survival of LBW infants, especially those weighing less than 2,500 grams. New technologies, procedures, and treatments have contributed to improved survival for these infants. However scientists also recognize the importance of delivering this care in an environment that fosters normal infant neurobehavioral development. NCNR's LBW initiative is striving to refine our understanding of infants' responses to stimulation and their need for restfulness in order to better plan and organize nursing care. Long term follow-up of LBW infants is necessary to better understand their developmental needs.

At the same time. however, research activity will be directed towards reducing the number of infants born each year below normal birthweight. Future research will test interventions designed to help pregnant women detect the early signs of premature labor and intervene appropriately. Further research is also necessary to help women of childbearing age adopt healthy lifestyles and avoid risk-taking behaviors which result in an unwanted pregnancy or a poorly developed fetus.

Advances in technologies available to monitor and analyze the physiological and behavioral changes in infants in the NICU have enabled researchers to address more complex issues regarding the care of these infants. One team of investigators is examining the effect of an individualized method of nursing care on infant outcomes, including physiological indices such as the shunting of venous blood through the foramen ovale and the delayed closure of the ductus arteriosus, as well as behavioral indicators such as feeding ability. Another group is using spectral analysis, which allows the analysis of multiple observations over time, to better understand the level of physiological arousal associated with the placement of infants in a skin-to-skin, chest-to-chest position with their mothers. This method of close contact may promote restfulness in infants as well as encourage the early development of healthy mother-infant relationships.

Promoting optimum uterine development and preventing premature labor are also important research goals. In one study, researchers are testing the effectiveness of augmenting routine prenatal care with frequent telephone contact by clinical nurse specialists in a population of rural low-income black women. Preliminary data suggest that heightened awareness and attention to the early warning signs of premature labor may permit timely interventions to reduce the number of early deliveries in this group. Another team of investigators is examining augmented prenatal care with a group of inner-city women at high risk for delivering low birthweight infants. This study will produce data not only about the effect of this prenatal care on mother and infant outcomes, but also about the cost of delivering such care.

HIV Infection: Nursing Interventions

Research on HIV infection has been designated as an NCNR priority in the National Nursing Research Agenda. Areas of concern include: prevention of transmission, physiological aspects of nursing care, psychosocial aspects of nursing care, delivery of nursing care, and support for caregivers. Populations of special interest for nursing research are: sexual partners of infected individuals, women of childbearing age, sexually active young adults, and minorities.

NCNR currently supports studies on physiological and psychological symptoms at different stages of HIV infection. The objectives of these studies are to determine quality-of-life measures, identify patient needs across different care settings, characterize the progression of the disease, and conduct HIV/AIDS clinical studies to develop effective interventions that will maintain optimal physiological and psychosocial functioning of infected individuals and their families across the spectrum of illness.

In addition, in collaboration with the Agency for International Development and other ICDs, NCNR is supporting an international study of behavioral interventions to prevent the spread of AIDS.

Rural Health

The special health care needs of individual residing in rural areas is the focus of an NCNR special initiative. Specifically, the health status of individuals, their health-care requirements, and the most effective methods of delivering health care to them are being addressed. NCNR's research portfolio in this area includes two research demonstration projects on community-based rural health care models for minority populations, as well as projects focusing on health care needs of the chronically ill elderly and issues surrounding care for pregnant women, including access to prenatal care. Furthermore, one of the new exploratory centers on adolescent health and behavior recently funded by NCNR will focus on rural youth. In particular, one investigator will examine the factors involved in the initiation and maintenance of tobacco use among rural teens.

Additionally, the NCNR recently convened the first meeting of the Rural Health Research Advisory Committee. This group consisted of scientists, clinicians, and other rural health experts and was asked to assist NCNR by defining issues in rural health care and research, identifying strategies for meeting the needs of clinicians and investigators involved in rural health, and to make recommendations for future activities. Areas of clinical concern that the group stressed were behavioral health problems, such as smokeless tobacco and alcohol abuse, mental health problems, such as depression, and occupational hazards, such as farm injuries and trauma to children working on family farms.

NCNR staff have also provided workshops and other consultation to rural health investigators in North Dakota, West Virginia, Wisconsin, and at a national rural health meeting in Washington state.

Caregiving Research

The caregiving burden and its effects on both patients and family members who provide care have been denoted as issues that cut across all of the priority areas specified in the National Nursing Research Agenda, the long-range plan for the NCNR.

Data suggest that caregivers experience extensive physical, emotional, and financial costs related to caregiving for the elderly and other individuals requiring special care at home. The majority of those who provide care, both professionally and among family members, are women. Although it is well documented that the care needs of older people at home can be extremely complex, little is known about the process of caregiving, the needs of the caregivers, or the outcomes for both patient and caregiver. In addition, there is little consensus about the conceptual, methodological, or clinical issues inherent in informal caregiving. The focus of NCNR's research will assess the impact of a wide variety of chronic illnesses and disabilities on older patients and caregivers. Such research includes the development and testing of social, behavioral, technological, environmental, and biological interventions that can affect patient outcomes and the caregiver role and the identification of actual caregiving behaviors needed to respond effectively to the changing physical and psychosocial needs of patients.

In addition to funding several projects on caregiving issues concerning older people in home and institutional settings, NCNR supports caregiving research related to patients who have Alzheimer's disease, cancer, cardiac disease, or hip fractures; children with chronic illness including AIDS; and ethnic differences in caregiving. An example of funded research includes a theoretical model that is being tested in two sites to explain caregiver perceptions of the caregiving burden and the quality of family caregiving for dependent elders in two ethnic groups, European-Americans and Mexican-Americans. This longitudinal study will assist in planning intervention strategies to assist families who are at high risk for providing poor quality elder care. Another study is testing the effects of a nursing Caregiving Support Program on the caregiver, the elderly care recipient, and the family. Home visits are supplemented by specific preparation for caregiving, a caregiving advice line, and a keep-in-touch system. Outcomes being measured in this study include caregiver role strain, health, anticipation of problems in assuming the caregiver role; care recipient satisfaction and use of health services; and family relationships and nature of the caregiver role. A third study funded by NCNR is testing the effects of two interventions on the social support, stress, and coping in caregivers of children with perinatal AIDS. Both interventions are implemented using the case management approach. One intervention is aimed at mobilizing the caregiver's social support network to effect problem solving, and the second intervention will utilize respite care. This longitudinal study will provide valuable information on how social support interventions facilitate effective coping and mitigate stress.

Research Training Initiatives

Nursing research programs are rapidly developing in many institutions of higher education. A strong cadre of nurse investigators is needed to address the complex problems related to improved patient care. Nurses, the majority of whom are women, need a variety of career options if they are to advance in science and build the knowledge base needed for improving patient care.

The research training and career development initiatives of the NCNR have several objectives: 1) to increase the total number of nurses who receive support for research training and career development, 2) to increase the number of nurse researchers in postdoctoral training, 3) to increase the opportunity for training in research-intensive environments through the support of institutional National Research Service Awards (NRSAs), and 4) to increase the number of minority investigators who receive research training and career development support.

Minority research training remains a priority initiative for NCNR. Several strategies have been initiated: 1) minority supplements to institutional NRSAs and minority faculty and student supplements to research awards--fifteen minority nurses were supported through these supplemental mechanisms in FY 1991; 2) workshops at historically black colleges and universities and minority schools of nursing; and 3) regular meetings of the Ad Hoc Committee on Minority Training for Nursing Research.

Postdoctoral preparation will be encouraged in FY 1993 especially in the biological sciences which can be interfaced with nursing practice concerns. A program announcement requesting research training individual and institutional applications for nurses studying in the biological sciences will be released in FY 1992.

Minority Health

The NCNR supports a variety of research projects focusing on minority health issues that cross-cut several NCNR programs. Several studies focus on black pregnant women in an effort to better understand social, cultural and biological variables linked to low birthweight. One study is addressing issues important to battered pregnant women, many of whom are African-American and Hispanic, while another is developing and testing a tool that women who live in a Southern rural area can use to monitor premature labor. Hawaiian pregnant women are the target population of another study which is identifying native beliefs and customs that can be utilized by health care providers to encourage women to seek the care they need during pregnancy. The NCNR supports a variety of other minority research projects that cut across several program areas. These include HIV infection prevention and control, rural health care of minority populations, and long term care of elderly populations.

National Center for Nursing Research

Intramural Research

Authorizing Legislation - Section 301 and 483-486, 487 of the Public Health Service Act. 1992 Authorization: Indefinite.

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
5	$550,000	9	$773,000	10	$812,000	+1	+$39,000

The Intramural Program of the National Center for Nursing Research continues its commitment to studying human immunodeficiency virus (HIV) infection in order to discover and expand biophysiologic and behavioral knowledge that improves the health of individuals with HIV infection, their families, and those who care for them. Ultimately, this knowledge promotes understanding of these health problems so that improved nursing interventions can be developed to treat health problems that occur as a result of HIV infection and its treatment. Such studies are increasingly important because the nature of HIV infection has evolved from a disease which was quickly fatal to one which is a chronic condition.

Funding for the intramural research program during the last 5 years has been as follows:

	Amount	FTE
1988	---	--
1989	---	--
1990	$231,000	2
1991	550,000	5
1992	773,000	9

Rationale for the Budget Request

The FY 1993 request for intramural research is $812,000, an increase of $39,000 over FY 1992. This amount will cover cost increases for centrally furnished services, laboratory supplies and services, and salaries. An additional FTE has been included for a nurse scientist in connection with expanded studies on health-related quality of life.

Currently, the NCNR is conducting a study of the type, severity, and causes of nutrition-related problems, such as unintentional weight loss, decreased appetite, and malnutrition, as well as the relationship between nutritional status and immune function. The subjects in this study are individuals receiving medical therapy for HIV infection through the AIDS and HIV-Related Research Intramural Program being carried out by the National Institute of Allergy and Infectious Diseases. A total of 90 subjects, 30 in each of three disease severity stages, is projected in addition to a group of female subjects. An additional symptom management study is comparing biopsy, blood, and functional features among individuals who experience muscle weakness after taking antiretroviral medication for prolonged periods.

Other NCNR HIV studies that are underway include: histologic, serologic, and clinical characteristics of myopathy occurring during prolonged antiretroviral therapy for HIV infection; a study of compliance in HIV infected people taking investigational drugs; and neuropsychiatric complications of interferon-alpha treated patients with histories of affective symptomatology or substance abuse.

The National Center for Nursing Research has joined with the National Institute on Aging and the National Heart, Lung, and Blood Institute to develop and conduct a study to describe predictors of caregiver burden in persons who care for elderly men with dementia and to describe the quality of life in these persons. Factors under investigation that are thought to contribute to caregiver burden and the quality of life among the female caregivers of these aging demented men include social support, coping strategies, health status, financial factors, and psychological factors. In addition, the men with dementia will be followed to document the relationship between deterioration of mental and physical status and the above factors. This study involves individuals selected from those already participating in the Honolulu Asian Aging Study, which is part of the overall project entitled the Honolulu Heart Program. The NCNR study focuses on the impact of caring for an individual with dementia on the provider. The NCNR component extends the nature and sphere of issues addressed by the original NHLBI and NIA studies. NCNR staff have developed the study protocol, pilot tested the methods, and are moving forward with data collection.

National Center for Nursing Research

Research Management and Support

Authorizing Legislation - Section 301 and 483-486, 487 of the Public Health Service Act. 1992 Authorization: Indefinite.

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
33	$3,558,000	39	$4,169,000	41	$4,373,000	+2	+$204,000

The research management and support activity is comprised of the Office of the Director, the Division of Extramural Programs, and the Office of Administrative Management, and provides leadership and management direction to the NCNR. Scientific and administrative staff work together to plan, develop and carry out Center-wide policies and programs.

The Office of the Director provides the leadership and guidance needed to manage the program areas of the Center. Its mission includes planning and evaluation, legislative liaison activities, scientific review, information dissemination, support to the National Advisory Council for Nursing Research, and liaison activities with other nursing organizations in and outside of the Federal government.

Three major areas comprise the Division of Extramural Programs (DEP): the Acute and Chronic Illness Branch, the Health Promotion and Disease Prevention Branch, and the Nursing Systems Branch. The extramural program provides scientific support and consultation for the Center's grant activities. The staff plan and develop scientific initiatives in areas that best achieve the goals of nursing research, manage the peer review process, report scientific information and serve in a liaison capacity for grantees and applicants.

Support for the administrative functions of the NCNR is provided by the Office of Administrative Management (OAM). In addition to coordinating with other offices and organizations, the OAM performs a variety of activities associated with the general business operations of the NCNR. The OAM includes the combined efforts of financial management, grants management, personnel management, and general administrative services.

Funding for the research management and support activity during the last 5 years has been as follows:

	Amount	FTE
1988	$2,017,000	25
1989	2,437,000	31
1990	2,820,000	26
1991	3,558,000	33
1992	4,169,000	39

Rationale for the Budget Request

The FY 1993 request for the research management and support activity is $4,373,000, an increase of $204,000 over FY 1992. This amount will cover increases for centrally furnished services, pay-related costs, and other supplies equipment, and services. Two additional FTE's have been included fc nurse scientist administrators in conjunction with the expansion of NCNR's extramural research initiatives in long-term care and women's health.

NATIONAL INSTITUTES OF HEALTH

National Center for Nursing Research

Detail of Permanent Positions

	FY91 Actual	FY92 Appropriation	FY93 Estimate
ES-4	1	1	1
ES-3	---	1	1
Subtotal	1	2	2
GS/GM-15	6	7	8
GS/GM-14	5	5	5
GS/GM-13	2	5	6
GS/GM-12	7	7	7
GS/GM-11	0	2	2
GS/GM-10	1	1	1
GS/GM-9	1	3	3
GS/GM-8	1	1	1
GS/GM-7	5	6	4
GS/GM-6	5	6	7
GS/GM-5	2	2	3
GS/GM-4	0	0	0
Subtotal	35	45	47
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	---	---	---
Director Grade	---	---	---
Senior Grade	1	1	1
Full Grade	1	2	2
Senior Assistant Grade	1	---	---
Assistant Grade	---	---	---
Subtotal	3	3	3
Unfilled positions end of year		0	0
Total permanent positions	39	50	52

NATIONAL INSTITUTES OF HEALTH

National Center for Nursing Research

New Positions Requested

		1993	
NCNR Research Management and Support	Grade	Number	Annual Salary
Nurse Scientist Administrator......	GS-13	2	$47,920

AMOUNTS BUDGETED FOR INCREASES IN FULL-TIME EQUIVALENTS

ACTIVITY/POSITIONS	GRADE	NO. OF POS.	O.C. 11 ANNUAL SALARY	O.C. 12 BENEFITS @ 20.0%	O.C. 21 TRAVEL	O.C. 23.1, 23.2 RENT	O.C. 23.3 COMM/ UTIL	O.C. 25 OTHER SERVICE	O.C. 31 EQUIPT.	OTHER OBJECTS	SUB.TOT. NEW COSTS	SUPPORT STAFF SHARE	NO.OF FTE	TOTAL NEW COSTS
NCNR Intramural Research														
Nurse Scientist (Staff Fellow)	GS-13	0	$42,000	$8,400							$50,400		1.00	$50,400
		0	42,000	8,400							50,400		1.00	$50,400
NCNR Research Management and Support														
Nurse Scientist Administrator	GS-13	1	47,920	9,584							57,504		0.80	46,003
Nurse Scientist Administrator	GS-13	1	47,920	9,584							57,504		0.80	46,003
		2	95,840	19,168							115,008		1.60	$92,006

Three new FTE's are requested in FY 1993 as follows:

- An additional FTE has been requested in the intramural program for a nurse scientist (staff fellow) in conjunction with expanded studies on health-related quality of life.
- Two additional FTE's have been requested in the research management and support activity for two nurse scientist administrators in conjunction with the expansion of NCNR's extramural research initiatives in long-term care and women's health.

National Center for Nursing Research

Advisory and Assistance Services

Consultant services continue to be of critical importance in carrying out the mandate of the National Center for Nursing Research (NCNR). The NCNR use of consultant services is primarily for the National Advisory Council for Nursing Research to provide scientific, medical, and technical expertise to the Center that are essential to the review process. By statute, their concurrence is required before most grant awards can be made.

Consultant services are also used to support contractual arrangements for the acquisition of services from outside experts for management and professional support services as well as specialized analyses and evaluations. In FY 1993, advisory and assistance contractual services are expected in conjunction with the priority expert panels which are developing the National Nursing Research Agenda, and a need for expert advice and assistance in the continued development of the Collaborative Intramural Research Program.

Internal Controls

Policy guidelines exist in the form of OMB Circular A-120 and DHHS General Administration Manual 8-15. Each year a consultant services plan is prepared identifying planned AAS procurements. The NIH accounting system contains Common Account Numbers (CANS) that have been designated for use in identifying and aggregating costs for AAS.

WEDNESDAY, MARCH 25, 1992.

NATIONAL CENTER FOR HUMAN GENOME RESEARCH

WITNESSES

DR. JAMES D. WATSON, DIRECTOR, NATIONAL CENTER FOR HUMAN GENOME RESEARCH

DR. BERNADINE P. HEALY, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. ELKE JORDAN, DEPUTY DIRECTOR, NATIONAL CENTER FOR HUMAN GENOME RESEARCH

DR. MARK S. GUYER, ASSISTANT DIRECTOR FOR PROGRAM COORDINATION, NATIONAL CENTER FOR HUMAN GENOME RESEARCH

JAMES C. VENNETTI, EXECUTIVE OFFICER, NATIONAL CENTER FOR HUMAN GENOME RESEARCH

ERIN S. BURGESS, BUDGET OFFICER, NATIONAL CENTER FOR HUMAN GENOME RESEARCH

DENNIS P. WILLIAMS, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTRODUCTION OF WITNESSES

Mr. NATCHER. At this time we take up the budget request for fiscal year 1993 for the National Center for Human Genome Research.

We have before the Committee Dr. Watson.

Dr. Watson, it is a pleasure to have you back before our Committee.

Before you give us your statement, tell us who you have with you at the table.

Dr. WATSON. On my left, Mr. James C. Vennetti, the Executive Officer for the National Center for Human Genome Research.

Next to him is Dr. Mark S. Guyer, Assistant Director for Program Coordination.

On my immediate left is Ms. Erin S. Burgess, our Budget Officer. On my right is Dr. Elke Jordan, the Deputy Director for the Center and then Dr. Healy and Mr. Williams.

Mr. NATCHER. Thank you, Dr. Watson.

We will be glad to hear from you.

OPENING STATEMENT

Dr. WATSON. Mr. Chairman, and Members of the Committee, this is the third time I have appeared before you as Director of the National Center for Human Genome Research, the component that oversees NIH's role in the Human Genome Project.

Now, in our second year of this 15-year, international project, it is my pleasure to describe to you some exciting accomplishments and lay out plans for the coming years.

55-258 O—92——20

GOALS OF THE HUMAN GENOME PROJECT

The main goals of the Human Genome Project are to develop maps of human chromosomes and other resources that will aid researchers in finding genes, and to determine the order, or sequence, of the 3,000,000,000 DNA subunits, called nucleotide bases, in the human genome.

We do this for two reasons. These genes provide the instructions for human existence. They provide the information which is the code for all the proteins in the human body. So by getting this information, we will have an enormous resource in understanding the human body.

The second reason is a very practical one: that some of these genes have been incorrectly copied in the course of the formation of the eggs and sperm and we have errant genes, which often give rise to serious genetic diseases.

We want to find the genes which lie at the root of these diseases, so the human genome program is a very practical program, which will have an enormous influence on the practice of medicine, not only for this next decade but for a long time.

I have been associated with genes for more than 40 years, so I am prejudiced about the project. But I think it is one of the most important projects carried out by NIH and by scientists throughout the world. When we have this instruction code, medicine and biology will never be the same.

So it is our real aim to get this done as soon as possible. There are too many people with now incurable genetic diseases, whom we want to help.

To find the nature of these diseases, in many cases, we have to find the genes. I was very pleased that I was part of the effort that brought NIH into the genome project, and I appreciate being chosen by former Director James Wyngaarden to lead the NIH program.

It was an honor to have this bestowed on me, and I take pleasure in it, not only by the fine staff assembled, but by the fine scientists involved in this project.

You can divide the goals of the project into three main components: The first is to get maps. Maps help to locate genes.

The second effort is to actually sequence these genes, find out their nature. And third goal of the program is to concern ourselves with the ethical, legal and social issues which will come about from having this genetic information.

We say this is the second year of the project. This may slightly confuse you because, in fact, this is the fifth year Congress has voted money for this effort—money specifically designed for NIH to participate in the human genome program.

That allowed Dr. James Wyngaarden to start a formal program. I was brought on to participate in the funding decisions in 1989. The initial years were spent really just moving into a position for action.

We felt that only by FY 1991 could we say that we really started the project. So our aim is to finish the project and we still believe we can do it in 15 years from FY 1991.

Now it is natural to ask, where have we come so far? We have had five years of funding. Have we done anything but spend money? I think we have accomplished a great deal. We have prepared a "report card" which shows the flow of progress.

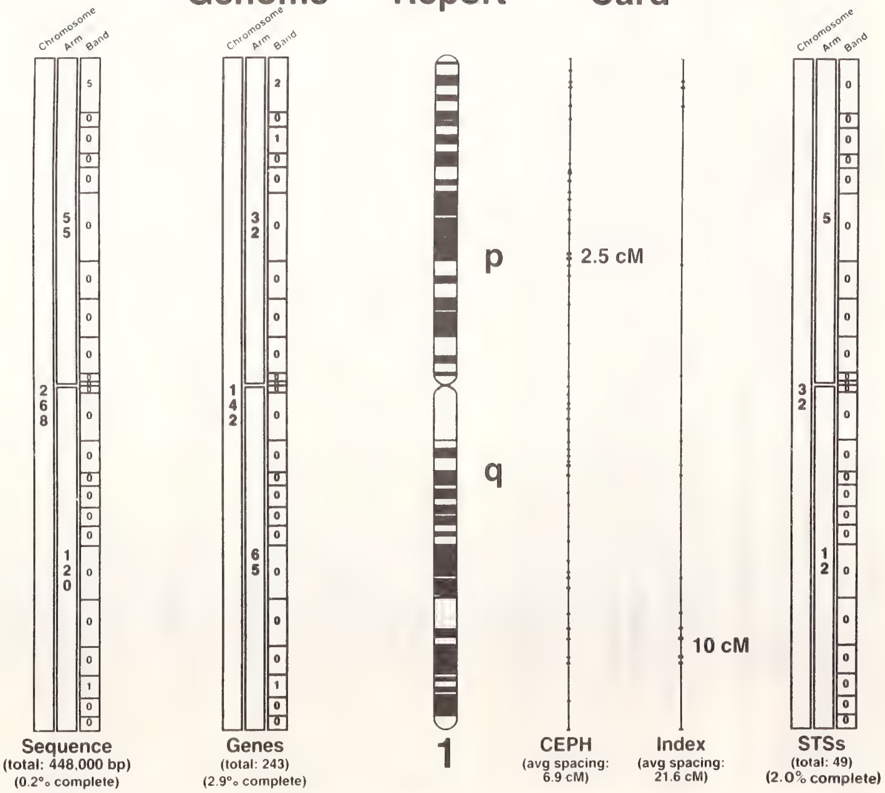
PROGRESS OF HUMAN GENOME PROJECT

I think this year is not perfect, but next year you will really see the enormous change.

If we can start out with the first chart, our report card: You can see here chromosome 1. There are 24 different chromosomes, but this is the way the biologist has traditionally seen it in a microscope.

[The information follows:]

Genome Report Card



We wanted to dissect this chromosome at different levels and show it at the level of the molecule that makes it up. The key molecule, the one that provides all the information, is the DNA molecule.

Each chromosome has one very long molecule. Next on this map is shown the location of the genes. We are putting together, along with scientists throughout the world, a genetic map.

Through genetic maps, you can locate genes. You can first say they are on this specific chromosome, but then you can get better and better genetic maps and locate the gene to a specific spot on the chromosome.

To get good genetic maps, you need good "index" markers. We have a three-year program to get a set of "index" markers which will allow us to map any genetic disease. If you divide the chromosome into 100 parts by placing 100 markers on it, the genetic map might get you within two or three of these markers, if you are locating genes along these chromosomes. We have located on chromosome 1, approximately 2 percent of the genes. Genes have been found in a variety of ways.

Finally, we want to get the sequence. That is working out the order of the base pairs in the DNA molecule. For chromosome 1, we have only about half a million base pairs. That is only two-tenths of one percent of the total.

So our main effort is to get the maps, to locate the genes and the final part of the project, one which will occupy the final 10 years of the project, will be to work out the region on the left-hand side of chart 1, the sequence.

Once you have the sequence, you will have essentially all the human genes. That is what we are trying to do.

The last diagram, on the extreme right of the chart shows markers which are generated when we are trying to locate and put together the physical maps. We do tiny little bits of DNA sequencing and get markers of sequence along the chromosomes. We call them sequence tag sites.

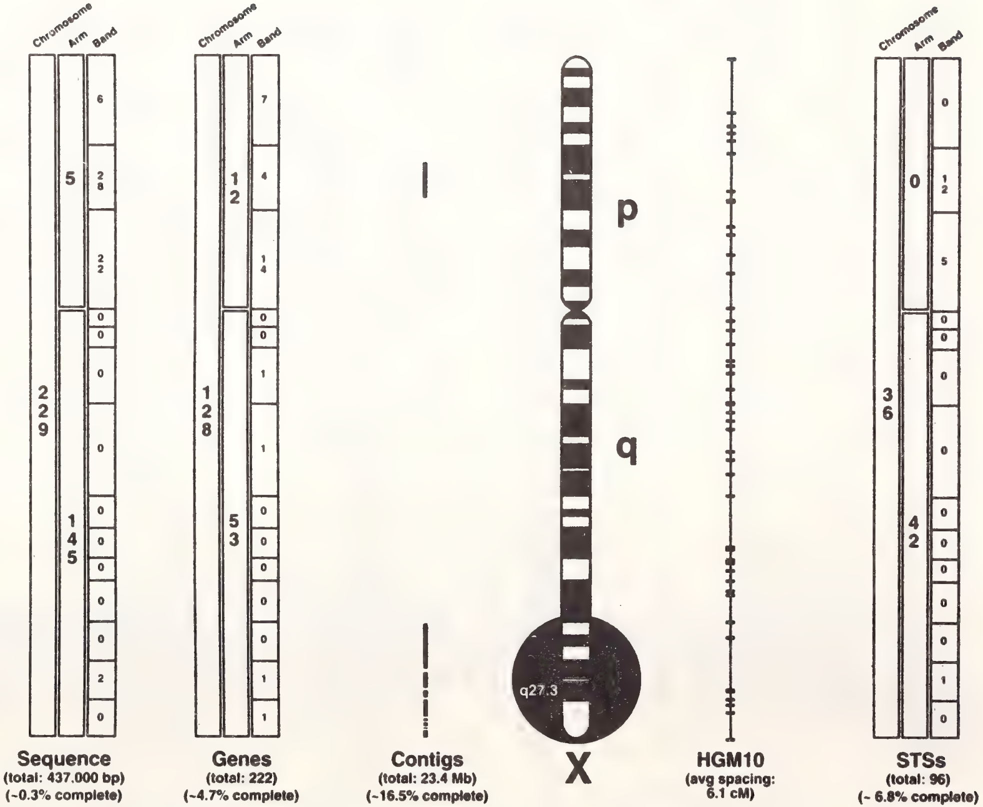
We have on this chromosome about 2 percent of these sequence tag sites done. That is an illustration of the types of maps and data we are developing and our progress so far on chromosome 1.

I want to go now to the chromosome where we have accomplished a great deal more. That is the X chromosome. We have two copies of this chromosome in women and one copy in men.

CHROMOSOME X

On chart 2, you can see there is a new component on this map which you did not see before. That is where we have physically begun to isolate the DNA.

[The information follows:]


Chromosome
Arm
Band
Sequence
(total: 437,000 bp)
(~0.3% complete)
Chromosome
Arm
Band
Genes
(total: 222)
(~4.7% complete)
Contigs
(total: 23.4 Mb)
(~16.5% complete)
p
q
q27.3
X
HGM10
(avg spacing:
6.1 cM)
Chromosome
Arm
Band
STSs
(total: 96)
(~ 6.8% complete)

So we now have the DNA to sequence. There are three stages in the process.

You have to get the piece of DNA that encompasses the gene and you have to sequence the gene. For the X, there are two contigs.

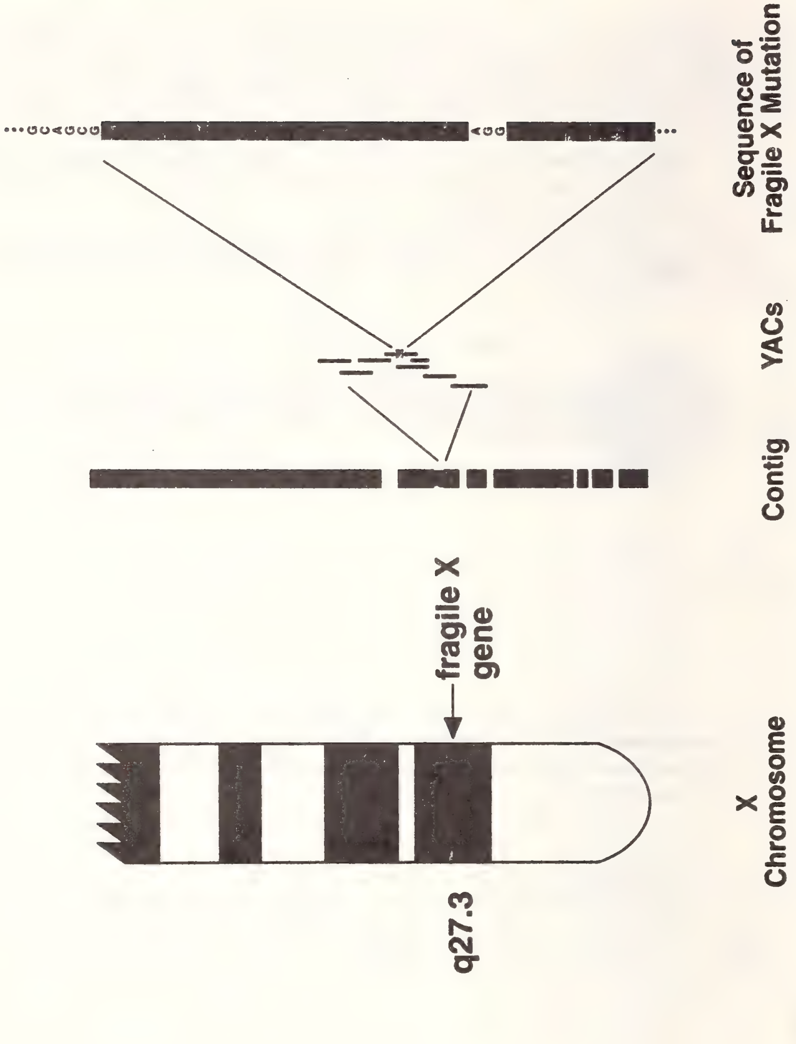
One is toward the bottom, and then another up toward the top. The top contig encompasses the DNA, which among other genes contains the gene for dystrophin, a protein which is damaged in boys with muscular dystrophy.

So people have started with the X chromosome because there are a large number of genes located on it and some are very important in studying diseases.

FRAGILE X SYNDROME

Now I want to concentrate on the bottom contig as we go to the next display, chart 3.

[The information follows:]



Sequence of Fragile X Mutation
•••GCAGCG
AGG
•••
YACs
Contig
fragile X gene
X Chromosome
q27.3

There has been a gene for a long time known as the Fragile X gene. This causes, in roughly 1 in 1,000 boys, severe mental retardation because of a defect in this gene. For more than 10 years there has been research by many scientists to find this gene.

At first they were unsuccessful. They were unsuccessful because there was so much DNA they didn't really know where to look.

So what the scientific community wanted to do was to put together pieces of DNA, which we call "contigs," which encompass the site where we knew from the genetic map that this gene resided.

So these pieces were isolated and they were isolated with the help of the human genome program. This is a project where if we had not been physically trying to get to the DNA, we would not have had success.

The first pieces of DNA were put together by Dr. Stephen Warren working in Georgia, and the bigger pieces were put together by Dr. David Schlessinger at Washington University, and then there were scientists in France who worked on it.

Similar pieces were isolated at Houston, Texas. They came independently to the discovery that this was a new type of mutation.

The so-called Fragile X chromosome, results from expansion in the gene so the gene becomes longer. It is relatively easy to find once you had some DNA.

The finding of the Fragile X gene is medically very important. First, it will enable genetic diagnosis of those boys who are mentally retarded and where you were unable to determine the cause. Now you can have a genetic diagnosis that is very firm.

In addition, if a child has been born into a family with this disease then it is possible to do genetic diagnosis for subsequent children. There have been various estimates of its cost, but it is roughly estimated that for every child that is born with this disease—every boy—it will cost in excess of $1,000,000 to take care of him over his lifetime. Because he cannot go to school and he cannot take care of himself, he will need to be looked after all his life.

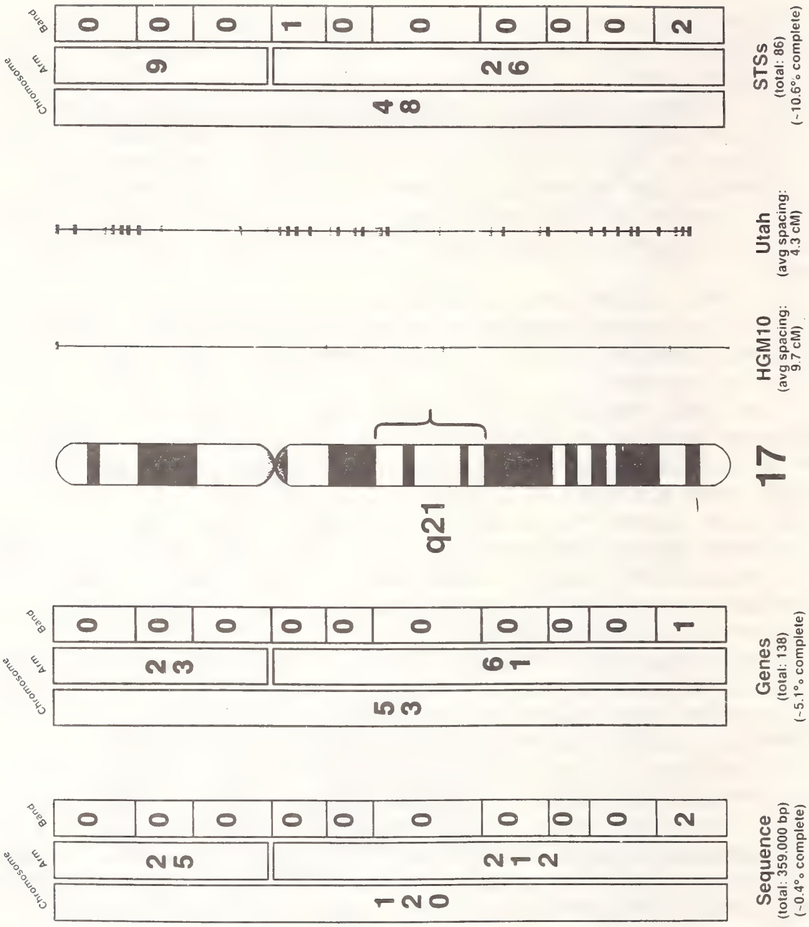
Even more recently the gene responsible for myotonic dystrophy has been found on chromosome 19. This is in adults. It is not as serious as Fragile X, but it can be debilitating. It was found by getting the pieces of the DNA in the region where the gene was. When we are able to isolate pieces of DNA and line them up along the chromosomes, we were able to find the gene. So I think it is very important to get the overlapping pieces of DNA for the chromosomes as fast as possible.

We now know how to do it. It is a function of the people involved and, of course, having intelligent people working on it.

BREAST CANCER—CHROMOSOME 17

The fourth chart is of chromosome 17. The reason there is interest is that the very talented geneticist, Dr. Mary-Clair King at the University of California at Berkeley, has mapped a gene that is responsible for early onset of breast and ovarian cancers. It is in a region designated as q21.

[The information follows:]


Sequence
(total: 359,000 bp)
(~0.4% complete)
Chromosome
Arm
Band
Genes
(total: 138)
(~5.1% complete)
q21
HGM10
(avg spacing: 9.7 cM)
Utah
(avg spacing: 4.3 cM)
STSs
(total: 86)
(~10.6% complete)

We don't know precisely where on that section of the chromosome, but there are very big efforts in our centers at Houston, Texas and Salt Lake City, Utah, to get lots of genetic markers for this region, isolate the pieces of DNA, and sequence the DNA in this region to find this gene.

Now if we find this gene, it should be possible to tell a woman when she is at risk from this particularly dreaded cancer. We can say that some of the very best "disease gene hunters" are now focusing on 17, on this particular region, to get the overlapping pieces and to see if they can get the gene.

Now I cannot tell you when we will have it but we hope within the next six months to a year. Given the fact that we now know how to do it, it is just a matter of focusing resources on it.

I think it is very important to find because breast cancer, if it is detected very early, can be cured. If a woman's mother dies of breast cancer or ovarian cancer, a daughter should feel she is possibly at risk.

When we have these genetic tests, in most cases, we can say either you are not at risk or in other cases we can say you may be at risk and should have frequent examinations to prevent a cancer from developing that cannot be cured.

So this is roughly the stage of the project. We think that we now have the possibility of accomplishing the physical and genetic mapping within the first five-year period of our program. From then on it is just to be able to find the genes.

ELSI PROGRAM

I should conclude by saying something about the other area of our program. If someone knows they are at risk for a serious disease, they could probably take a test which might be paid for by an insurance company. So you have the whole question of privacy of medical information.

I think we have to have absolute guaranteed genetic privacy. To study the issue, we have assembled what we call our ELSI Program—Ethical, Legal and Social Implications Program.

We started out by spending 3 percent of our money on this program. This year we are spending 5 percent on it. I think as we find more of these genes, the ethical issues will increase.

I would not be surprised that five years from now this area will be 10 percent of our budget. Besides the privacy issue, we have the whole question of insurance, and not allowing people to be discriminated against.

Then we have the general issue that the people using this information need to understand it. We have to make the American people genetically literate. So there will be an educational campaign which we are beginning to develop.

We cannot do it all by ourselves. I am proud of all components of the human genome project, but I am particularly pleased with what we have done with the ethical issues.

We have an outstanding group of people who are discussing these issues. The people on this Committee are potential users of this genetic information, not the providers.

We try to get those people who think they may be at risk, not the providers, to be on the committee. I guess in time everybody will worry about their genes, but we focused on those people for whom there is a threat of discrimination to let them come up with their recommendations.

Our timetable for that is we want two years to work on the issues of privacy and insurance. I think we have the hope that in doing this, working with law enforcement agencies, working with the insurance industry, we will have acceptable recommendations.

It is not a confrontational thing. I think these are issues which essentially cut across all classes, and economic and racial groups.

Everyone suffers from genetic problems. I think we found remarkably good results on all sides in trying to come to grips with problems that are not easy. We can never totally repair the effect of somebody having a serious genetic disease, but we have to work together to prevent the development of any form of genetic discrimination. We have to be concerned about discrimination.

So our committees are proactive. We are not just writing words. We are working to see recommendations developed and implemented.

If you ask the question, How do we know our ethics program is good? I think we will only know that we have succeeded if there are not such serious misuses that there are Congressional hearings on this—hearings on loss of privacy. If there are scandals, our program has failed to work. But we want to move on this.

In conclusion, Mr. Chairman, the budget request for the National Center for Human Genome Research for fiscal year 1993 is $110,429,000.

I will be happy to answer your questions.

Mr. NATCHER. Thank you, Dr. Watson.

[The statement of Dr. Watson follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement of the Director
National Center for Human Genome Research

Mr. Chairman and members of the committee, this is the third time I have appeared before you as director of the National Center for Human Genome Research, the component that oversees NIH's role in the Human Genome Project. Now in our second year of this 15-year, international project, it is my pleasure to describe to you some exciting accomplishments and lay out plans for the coming years.

The main goals of the Human Genome Project are to develop maps of human chromosomes and other resources that will aid researchers in finding genes, and to determine the order, or sequence, of the 3 billion DNA subunits, called nucleotide bases, in the human genome.

As research results have now begun to flow, we have developed a "report card" to keep track of progress toward our goals for mapping human chromosomes. This report card shows the gains we have made on each chromosome in the areas of genetic mapping, physical mapping, DNA sequencing, and gene discovery. Today, I am pleased to give you our first report card to serve as the baseline. By comparing future editions of the report card with the current one, we will be able to see exactly how much progress is being made.

In the past year, the research tools we are developing have already helped to isolate disease genes. In particular, the discovery of the gene for Fragile X Syndrome illustrates ideally how all the phases of a gene hunt fit together. The discovery of the Fragile X gene was an international effort, and NCHGR-supported investigators made key contributions to the search. Fragile X Syndrome is an inherited disorder and the most frequent cause of mental retardation among males. Boys who develop this disease have a weak point in their X chromosome, which causes the tip of the chromosome to hang by a thread. Scientists around the world have been on the trail of the Fragile X gene for several years. Their first big break came when Dr. Stephen Warren at Emory University School of Medicine, in Atlanta, Georgia, prepared special cell lines, which allowed researchers to narrow the location of the gene to a specific region on the X chromosome. Researchers then began isolating cloned DNA pieces from the region on chromosome X where the gene defect was located. Dr. David Schlessinger, at Washington University in St. Louis, had been making YAC clones in his work to develop a physical map of the X chromosome. YAC cloning uses yeast cells to isolate large pieces of human DNA for chromosome mapping. One of these YAC clones contained the piece of DNA that spanned the region where the Fragile X gene resided. Scientists in the United States, Europe, and Australia then sequenced the DNA from that region and were able to spot the mutation. The error turned out to be a long duplication of a small number of nucleotides in the gene.

Physical maps of human chromosomes are important tools in this approach to finding genes and have played a key role in isolating genes involved in several genetic disorders, besides Fragile X. These include an inherited form of colon cancer; Charcot-Marie-Tooth Syndrome, a degenerative disorder of the nervous system; and Kallman Syndrome, which is characterized by an unusual group of symptoms. The critical role physical maps play in enabling scientists to fish genes out of enormous stretches of DNA has made them a high priority of the Human Genome Project.

This past year, we have made great strides in physical mapping of human chromosomes. Dr. Schlessinger and his coworkers have almost completed the map of a region 50 million bases long at one end of the X chromosome. This region is about the same size as the smaller human chromosomes, and represents 1.5 percent of the human genome. The map includes a single set of overlapping DNA pieces, called a "contig," 8 million base pairs long, far longer than the goal of 2 million bases established for contigs in the five-year plan. Significant physical mapping programs have now been established for about half of the 23 human chromosomes. However, reaching the five-year goal for most of the genome still poses a significant challenge. To meet this goal, we will need to find more efficient ways to assemble physical maps and to initiate physical mapping projects on additional chromosomes.

Excellent progress has also been made on another important kind of map, the framework genetic map I described to you last year. This project was begun to establish quickly a set of high-quality markers on all the human chromosomes and get them in the hands of the research community as soon as possible. These markers are essential tools needed in the first step of a gene hunt. Underway for less than a year, the project has already identified about 300 markers, which is about half of what we need to finish the map. We have prepared a catalog of information about these markers, which is being distributed to the research community.

Improved markers on genetic maps have also led to important discoveries. This past year, Dr. Mary-Claire King, at the University of California, Berkeley, used such markers to rapidly identify a region of chromosome 17 where a gene for an inherited form of breast cancer is located. Now work is underway in Dr. King's laboratory and at NCHGR-supported genome centers to find the exact location of the gene and to isolate it for analysis. Isolating the breast cancer gene will give scientists new insights into the fundamental cause of this tragic disease. It will also help to develop a diagnostic test to identify women at high risk for breast cancer so they can avoid factors that contribute to the disease or begin treatment early, when chances of survival are greatest.

Detailed physical maps provide researchers with the starting point for sequencing the human genome. Sequencing means working out the order of the nucleotide bases of the DNA molecule. The technique will allow us to decipher the biological instructions encoded in genes. It will help us examine large stretches of DNA to pinpoint which parts encode proteins and which parts carry out other functions. The five-year goal for DNA sequencing is to lower the cost and increase the efficiency of sequencing methods, which are currently too expensive and too slow to sequence the human genome.

NCHGR has initiated several projects to improve existing sequencing techniques or come up with completely new ones. Experiments designed to push the limits of existing technology through automation and improved efficiency, will focus on the genomes of important research organisms, as well as selected regions of human DNA. An international team headed by Drs. Robert Waterston at Washington University in St. Louis and John Sulston at the Medical Research Council in England, have set a 3-year goal of sequencing a 3-million base pair portion of the DNA of the roundworm. The size of the worm's genome is about 100 million base pairs, close to an average human chromosome. In the first year of that project, the team has sequenced 220,000 base pairs, which is ahead of their own expectations. The sequence has already revealed a large number of new and unsuspected genes, many of which are similar to genes of more complex organisms. This information will help researchers decipher the functions of genes across the evolutionary tree.

Similar results have been obtained in two other NCHGR-supported projects. Dr. Fred Blattner, at the University of Wisconsin, has recently completed the sequence of a 91,000 base-pair stretch of DNA from the bacterium *E. coli* and identified in that stretch 80 potential genes. Thirty-eight of these appear to be newly discovered genes, which had not been previously uncovered by other gene-finding techniques.

Dr. Leroy Hood, at the California Institute of Technology, is studying the organization and function of a large region of human DNA that contains the genes for the T-cell receptor. This set of proteins, which sits on the surface of white blood cells, plays an important role in the immune system's ability to recognize and fight off foreign invaders in the body. Dr. Hood has sequenced over 50,000 base pairs from the human T-cell receptor gene region and 90,000 base pairs from a similar region in the mouse. Through these studies, he has improved sequencing technology and also made great strides in identifying DNA segments responsible for T-cell receptor diversity. As these sequencing projects complete their first phase of technology development, they will focus on producing large amounts of sequence in FY 1993 and see how much further cost can be reduced.

NCHGR is also supporting research into the next generation of DNA sequencing methods. Using electrophoresis gels as thin as a couple of sheets of paper, Dr. Lloyd Smith, at the University of Wisconsin-Madison, has developed a method to increase significantly the speed of separating base pairs in the sequencing process. Using conventional gels, a laboratory worker can run only one in an 8-hour day. With this new technology, a gel can be run in an hour. Dr. Smith is experimenting with automating ways to load samples on the ultra-thin gels, which would further reduce the time it takes to run them.

The Human Genome Project includes in its objectives the study of a few model organisms. In addition to *E. coli* and the worm, substantial progress has also been achieved in two other organisms. Dr. Dan Hartl, at Washington University in St. Louis, has been engaged in an aggressive effort to develop physical maps of the fruit fly genome, and the genome center at the Massachusetts Institute of Technology has produced a genetic map of the laboratory mouse that is approximately one-third complete.

The ability to store, access, and analyze research information by computer is now central to the success of genetics research. This past year, in collaboration with the Department of Energy human genome program, NCHGR funded the Genome Data Base (GDB) housed at Johns Hopkins University in Baltimore, Maryland. Currently accessed by more than 3000 researchers worldwide, GDB collects, edits, and distributes data about human chromosome maps. GDB offers a very important focal point for international collaboration, and we are engaged in discussions to make the management and funding of GDB international as well. NCHGR is currently seeking to establish similar databases for information on the mouse, yeast, and fruit fly genomes.

Other community services supported by NCHGR include screening of YAC clones containing DNA from human chromosomes 17 and 21. Investigators from smaller laboratories, which do not have the resources to develop and screen YAC libraries, can send their DNA markers to our screening laboratories to obtain larger, cloned pieces of DNA containing their markers for study. NCHGR also supports laboratories that provide mapping services so that investigators can zero in on the physical location of a gene or piece of DNA they are studying. In addition, NCHGR supports three "visitor's benches" to help gene hunters who do not have access to all the diverse and most efficient technologies to find the genes they are looking for. Laboratories at Stanford University, Roswell Park Cancer Institute, and the University of Utah have devoted lab space and staff time to visiting scientists who want to use the laboratories' expertise and materials to find genes.

Access to DNA samples contained in cell lines from extended families is crucial to successful genetic linkage mapping. This year, NCHGR continued to support the transfer of the world's largest set of these cell lines, maintained at the Centre d'Etude du Polymorphisme Human, in Paris, France, to a public repository in Camden, New Jersey. Now the cell lines are available to any scientist who is interested in using them. Similarly, researchers at Howard University in Washington, D.C., have been awarded a planning grant to establish a set of cell lines from African-American families to add to the resources for genetic mapping. Such resources can be useful in identifying genetic differences in subpopulations, which may account for differences in disease risk or physiological responses to environmental factors.

The Ethical, Legal, and Social Implications (ELSI) Program has been active this year in pursuing its research goals. In a major, 3-year study begun this fall, NCHGR, in collaboration with two other NIH institutes, is supporting research aimed at understanding the social, clinical, and public education aspects of carrier testing programs for genetic diseases. Seven research teams across the country will offer DNA testing for cystic fibrosis (CF) mutations in healthy adults. Healthy people who carry one copy of the CF gene are referred to as "carriers" because they do not develop CF but may pass it on to their children. These studies will help health care professionals understand the best way to educate and deliver genetic tests to patients who ask for them, especially as the number of new genetic tests continues to grow. In FY 1993, NCHGR is hoping to collaborate with the National Cancer Institute to begin similar kinds of studies of genetic tests for colon and breast cancer.

The budget request for the National Center for Human Genome Research for FY 1993 is $110,429,000. Mr. Chairman, I will be happy to answer any questions you or other members of the committee might have.

CURRICULUM VITAE

Name James Dewey Watson

Birthdate: April 6, 1928 - Chicago, Illinois

Education: 1947 - B.S., Zoology, University of Chicago
1950 - Ph.D., Zoology, Indiana University

Professional Career:

1950-51	Research at the University of Copenhagen with H. M. Kalckar
1951-52	Research at Cambridge University in the Cavendish Laboratory
1953-55	Senior Research Fellow in Biology, California Institute of Technology
1955-56	Research at Cambridge University in the Cavendish Laboratory
1956-58	Assistant Professor of Biology, Harvard University
1958-61	Associate Professor of Biology, Harvard University
1961-76	Professor of Biology, Harvard University
1968-	Director of the Cold Spring Harbor Laboratory
1988-89	Associate Director for Human Genome Research, NIH
1989-	Director, National Center for Human Genome Research, NIH

Awards:

The John Collins Warren Prize of the Massachusetts General Hospital (with F.H.C. Crick), 1959; Eli Lilly Award in Biochemistry, 1960: Albert Lasker Prize (awarded by the American Public Health Association), 1960; Research Corporation Prize (with F.H.C. Crick), 1962; Nobel Prize in Medicine (with F.H.C. Crick and M.H.F. Wilkins), 1962; John J. Carty Gold Medal of the National Academy of Sciences, 1971; The Presidential Medal of Freedom, 1977

Honorary Degrees:

D.Sc., University of Chicago, 1961; D.Sc., Indiana University, 1963: L.L.D., Notre Dame University, 1965: D.Sc., Long Island University (C.W.Post), 1970; D.Sc., Adelphi University, 1972; D.Sc., Brandeis University, 1973; D.Sc., Albert Einstein College of Medicine, 1974; D.Sc., Hofstra University, 1976; D.Sc., Harvard University, 1978; D.Sc., Rockefeller University, 1980; D.Sc., Clarkson College, 1981; D.Sc., State Univ. of New York, Farmingdale 1983; M.D., Buenos Aires, Argentina, 1986; D.Sc., Rutgers University, 1988; D.SC., Bard College, 1991

Professional Affiliations:

American Society of Biological Chemists; American Association for Cancer Research

Honorary Affiliations:

American Academy of Arts and Sciences (1958); National Academy of Sciences (1962); Danish Academy of Arts and Sciences (1963); Honorary Fellow, Clare College, Cambridge University (1968); American Philosophical Society (1977); Atheneum (London) (1980); Royal Society (London) (1981); Academy of Sciences (USSR) (1989)

PROGRESS OF THE HUMAN GENOME PROJECT

Mr. NATCHER. Now, Doctor, this is the fourth year, as you know, that we will have funded the genome project as a separate center. Generally speaking, is the project as far along as you think it should be at this point?

Dr. WATSON. Yes. I think we are just about on track.

Mr. NATCHER. In your opinion, is the genome project turning out to be more or less important to science than when it was first conceived?

Dr. WATSON. I think there is increasing influence in the scientific community for the project. Two years ago I was running around the country defending it.

This year no one has really asked me to defend it. In the sense that, I think, the fears in the scientific community that this was going to divert resources away from more important areas have for the most part vanished.

As an example, there is a very talented group of scientists studying the tiny fruit fly, drosphila. They originally said they didn't need the Human Genome Project. We have just had an application from them. They are now very enthusiastic about the Human Genome Project.

They want us to help them work out the genome of drosphila. We are in favor of that for the very simple reason that genes are related from the most simple organism to the most complex organism. Working on drosphila will help identify other genes. The scientific world I move in is quite enthusiastic for the project, and I am not having to defend it.

TOTAL COST OF THE HUMAN GENOME PROJECT

Mr. NATCHER. Dr. Watson, have you had reason to revise your estimate of the total cost of the genome project, which you have previously testified would be $3,000,000,000?

Dr. WATSON. No. I think the real cost of the project comes from finding the genes by doing the DNA sequencing. We said we don't want to start this large scale sequencing until we reduce the cost to 50 cents per base pair. That would be $1,500,000,000 for the completion of the project.

We are starting pilot projects of DNA sequencing to see how much it will cost when we put together fairly large groups.

Our most successful effort is at Washington University at St. Louis, working together with very talented scientists from the UK, they are quite confident of their success and we would like to give them more money so they can move up to production mode.

The cost would be in proving what they can do. Can they bring the cost down to the estimated $1.00 a base pair. It may mean putting off massive sequencing for a year or two before you get the cost down, but you are not going to hear someone complain to Congress saying the Human Genome Project is going to cost you $4,500,000,000 or $6,000,000,000.

PATENTING DNA SEQUENCES

Mr. NATCHER. Dr. Watson, what do you think of NIH's decision to seek patents on several thousand gene sequences?

Dr. Watson. The patent law really doesn't cover DNA. It was invented before DNA was discovered. There is the possibility that, in fact, DNA can be patented. That will be decided by lawyers and judges.

The second question is, if it is patentable is that a good thing for the human genome biotechnology industry? This is a debatable issue.

I think it would be better if we did not patent sequences that you don't understand. Once you understand what it does, then I am in favor of patenting.

I am not a lawyer. I am not responsible for this decision.

I think you should ask Dr. Healy her views on this point.

Mr. Natcher. Dr. Healy, how do you feel about it?

Dr. Healy. I think the debate on DNA patenting is inevitable. Every time we have moved into the issue of patenting some aspect of genes, trans-genic animals, genetically engineered microbes, and so forth, there has been an enormous debate and question.

I think a debate on DNA, for which we have limited knowledge, was inevitable. NIH policy has been, after many months of considerable discussion and review of the issue, to take what we view as a protective posture. It is not to make a statement as to whether or not it is good or bad to hold a patent on this material under these circumstances, but rather a position that, until we have a position of legal harmony and legal certainty, until we have international agreement on what is patentable and what is not, and until we know what the consequences of the patenting or licensing would mean and what it means if this information is put in the open literature without any kind of intellectual protection; until those issues are resolved, NIH is taking a protective posture.

Now this is an interim decision on the part of NIH. We are planning to have a series of meetings and discussions which involve aspects of not just the scientific community, since this is an issue that also involves the citizenry at large and industry. It involves all commerce and public citizens.

And it certainly involves the international community. Until we have adequate dialogue, and until we are prepared at a level higher than NIH to come up with a permanent policy decision, I think we will go with where we are now.

Mr. Natcher. Mr. Pursell, I yield.

STAFF INCREASES

Mr. Pursell. Thank you, Dr. Watson.

I had an opportunity to tour your laboratory last year. You and I were talking about your facilities and your staff.

You are asking for additional staff this year; correct?

Dr. Watson. Yes, we are asking for about six more people.

Mr. Pursell. What kind of staff would that be that you need?

Dr. Watson. Both scientists and administrators. We have to increase the number of people working on the program. We now have 45 people in our office.

RESEARCH CENTERS

Mr. PURSELL. You also have 12 centers. It went from 9 to 12 and we are at 12 now; correct?

Dr. WATSON. We anticipate having 12 in FY 1992 and FY 1993. We have seven very active human genome research centers right now along with the biotechnology center and one exploratory center.

Right now we are in the position of asking ourselves what is the optimum size of a human genome research center to do the various tasks.

We started out thinking the optimal size, at least to start with, was between 20 and 30 people, with a budget to somewhat under $3,000,000.

Mr. PURSELL. In those centers, are you comfortable that we have highly-qualified scientists in the country to help with the long-term project?

Are we short of scientists?

Dr. WATSON. I could not think of a better place to put a center than Ann Arbor, and they certainly have a fine staff.

AVAILABILITY OF GENOME SCIENTISTS

Mr. PURSELL. I am aware of that; I support that. Are there scientists coming up in the younger generation to fill the needed roles as we continue in the long term?

Dr. WATSON. I think so. You don't get as many new people like Dr. Francis Collins, Director of the Michigan Human Genome Research Center. I should say you are lucky if you get one a generation. Overall, the quality of people at all the centers is extremely good.

The institutions which came in with applications were some of the best in the country. It is my impression when you have a big program, you have to be very careful with the people you hire to get only the best.

The group at Salt Lake City is outstanding, at Baylor, they are outstanding, the San Francisco group is outstanding, we also have a very fine center at MIT. The question will come up, do we want to make these centers bigger or create additional ones? That is under active negotiation.

What is clear is the relative amount of money we want to spend in the centers will increase because when we have a center it means they know how to do the task and we want to get the job done.

RESEARCH CENTERS

Mr. PURSELL. Would we improve or expand the existing centers rather than get new centers?

Dr. WATSON. I think we will probably go in both directions. What we have been finding is that the existing centers are asking for supplemental funds.

We are very pleased because it means that they are succeeding. We set them up with a five-year grant. We will have a very serious review after three years. But I would say of the ones now into their second year, they are all quite successful.

The first year, in many cases they had to renovate facilities. In many cases, the universities paid for it, but they had to go through several university review processes.

In the second year, they are going full blast. I know the people at St. Louis, Washington University, would like to increase the size of their center.

We have to say to them, should you increase your size? We were wary but the French decided to put all their money into one large laboratory outside of Paris. That laboratory is called Genethon.

INTERNATIONAL COLLABORATION

Mr. PURSELL. Are we in the lead?

Dr. WATSON. I think, through Genethon, the French have moved into super production first. We have an effort at super production at MIT, getting the genome of the mouse. The mouse is similar to humans and you can learn an enormous amount by working with mice.

The French are in very active discussions with all our center directors.

Dr. Mark Guyer will be going to Genethon next week. Virtually all the techniques Genethon has been using were worked out in American labs.

Mr. PURSELL. So we are more on the cutting edge than other countries today?

Dr. GUYER. Definitely.

Mr. PURSELL. What is the number two country? Who is close to us or working with us?

Dr. WATSON. France. Also important are the U.K. and Japan.

The Japanese really just announced an effort. It is much less coordinated than the effort in the United States. NIH and DOE work closely and satisfactorily together.

All of our committees are joint NIH–DOE committees and that is working well.

The Japanese have four different funding sources. So far these different sources have not cooperated with each other. One of our advisers was in Japan 10 days ago. He said there is still infighting. Don't panic by what is being done in Japan.

However, we know with time they will have a very serious DNA sequencing effort. We should not be complacent.

The French are also putting quite a bit of money into the technology. I think we are all united by the goal of completing the job as soon as possible.

I look forward to working with all countries of the world.

Mr. PURSELL. Thank you, Mr. Chairman.

Mr. NATCHER. Mr. Stokes.

ELSI PROGRAM

Mr. STOKES. Doctor, this morning in your presentation you made reference to certain ethical, legal questions, the whole matter of privacy, et cetera.

It is conceivable that the right of privacy may conflict with the interests of insurers, employers, courts of law, and a whole panoply of issues I can think of legally?

To what degree is the Center considering all these of issues?

Dr. Watson. I think we are considering them all in considerable detail, not only through our Program Advisory Committee, but through a series of grants we awarded. We commissioned an extensive report on privacy—how you safeguard genetic information. We hope to have the complete report in two years.

We commissioned another report on the insurance aspects. That falls into two areas: health and life insurance.

I think it will be much easier to protect against discrimination in health insurance than it will be for life insurance. Personally, I believe every American has the right to adequate health care.

The question of what right you have to life insurance is more complicated. Does someone have the right to have a $5,000,000 life insurance policy and to be able to genetically test themselves without the insurance company knowing? These are the sort of issues which need to be discussed.

We have not had an adversarial relationship at all with the insurance representatives. It is just my own personal belief that it is in their self-interest not to be tarnished by controversy.

There are isolated cases where people have not wanted to have genetic tests paid for by an insurance company, because if the test came out wrong, they felt that would put them a risk of losing health insurance.

I think this issue is going to have to be settled by law or in the type of health care system that evolves in the United States.

As I have said, we have tried to have our committees composed of users, not the providers, so those of us who are working on the basic biology side of the Project are not on the ethics committee. We have tried to encompass people who are not at the center of American thought, you know, conventionalism.

Mr. Stokes. It also would seem to me that the use of genetic information could conceivably lead to discrimination in employment or health care coverage, which we referenced, or it could stigmatize individuals socially. Are these types of concerns being addressed?

Dr. Watson. Very seriously, yes.

If you have a parent who dies of Alzheimer's at age 50, it is probably genetically determined and it means you have one chance in two of also coming down with Alzheimer's. Now you have problems.

If you know this disease is in your family, do you tell the person you want to marry? So we already have these problems.

What diagnostic tests are going to do is allow health care providers to be more precise. Where there is now an estimated 50 percent chance, the tests will be able to say what the chance is with certainty.

There is also a real question about whether people want to know. I personally would probably want to know. So you don't want a situation where any one person is forced to take genetic testing.

Informed consent is a tricky matter. People many times don't know what they are signing. So the whole question of trying to make the American public genetically literate is very important.

The Cold Spring Harbor Laboratory, where I also have a position, has a program trying to deal with DNA education at the fifth grade, with the thought that we should educate individuals early. We don't want to wait until they get into college.

We want to get the average American knowledgeable about genetics. This program will soon be started where scientists go into the minority districts in New York City and talk to students at the 10-year-old level and ask them, why do the children in the family look different? And explain it is because of their genes.

They hope to get the students to appreciate the origin of this variability and what it means to be a carrier of sickle cell anemia. To be a carrier does not mean much to the person who is a carrier but it could affect the offspring.

These are issues where we have to educate the people. I think the education in genetics has to start in the elementary school.

Our ELSI program is beginning to be concerned about education. I say the budget for the ethical, legal and social implications program will increase. It will have to increase if we are going to provide a vast amount of genetic information which is not going to confuse the public, which cannot be misinterpreted and lead to cases of discrimination. We can't just pass laws. We have to educate the people.

Having laws with the absence of education about what the genes are, will probably cause mistakes in the application of laws—mistakes made by people who will get themselves tested for things they cannot do anything about.

We have to take a very proactive role. I discovered when I go around the country and give talks—and next week I am going to the University of Iowa for an ethics symposium—the key issue people want to talk about is potential discrimination and privacy.

I think the human genome program should be headed by someone who knows that it is the chief issue about which the American public is concerned. We not only want to use the information to help cure breast cancer, but we want to make sure we avoid discriminating against people in employment because they may be at risk for early ovarian cancer.

These are not easy issues. But Alzheimer's and ovarian cancer are not nice things, so in attempting to do something about these diseases, we do not want to create problems.

I think the net effect will be a big plus, but it will not be a big plus without great effort.

Mr. STOKES. Thank you.

Mr. NATCHER. Mr. Early, I yield.

INTERNATIONAL COLLABORATION

Mr. EARLY. Dr. Watson, how much is France spending?

Dr. WATSON. We estimate the figure for 1993 to be $18,000,000.

Mr. EARLY. The U.K.? I am not holding you to these numbers.

Dr. WATSON. $8,000,000.

Mr. EARLY. Twenty-one?

Dr. WATSON. Yes, $21,700,000 in Japan.

However, U.S. figures include the salaries of investigators. When you get to Europe, scientists are already working for the government and their salaries are covered in another budget category and not included in the dollars spent on genome research.

TECHNOLOGY DEVELOPMENT

Mr. **Early**. I have several layman's questions on your statement. What is the importance of technology, for progress in genome research?

Is there any collaboration with the National Center for Research Resources on technology development or the application of existing technologies?

Dr. **Watson**. We are spending about $20,000,000 of our $100,000,000 on technology development.

Mr. **Early**. Why don't you expand on that for the record—in layman's language.

Dr. **Watson**. All right.

We have numerous contacts with a large number of industrial companies.

[The information follows:]

Technology Development

The NCHGR administers an ambitious program in the area of technology development. In FY 1991 the allocation for technology development was $13.5 million. These funds supported development efforts in the areas of physical mapping, $5.7 million, linkage mapping, $2.3 million, and DNA sequencing, $5.5 million. In addition, the NCHGR supports feasibility studies for large-scale DNA sequence analysis, each of which contain significant technology development programs.

Recently the NCHGR has increasingly utilized developmental grant mechansims to support technology development. The R21 grant provides up to two years support for investigators to test the feasibility of new technologies. The P20 grant, which provides up to three years of support, is designed to encourage the development of interdisciplinary approaches to new technology.

Through the use of these mechanisms the NCHGR has invited the participation of corporate as well as academic scientists. In addition, encouragement has been provided to engineers, chemists, and mathematicians, as well as molecular biologists.

In response to congressional appropriation language, the NCHGR issued a Request for Applications for New DNA Sequencing Technology Development in Support of the Human Genome Program. The scope of research supported by this RFA includes:

The development of new sequencing methods that will allow large-scale sequncing of DNA at a cost significantly below 50 cents per base pair, or

The improvement, by at least 10 fold, of current sequencing methods which are robust enough for large-scale DNA sequencing.

Through this RFA, researchers with scientifically sound approaches which can be high risk, high payoff, were encouraged to participate in DNA sequencing technology development.

INFORMATION DISSEMINATION

Mr. **Early**. I want to know about information dissemination. Carl has concerns and I have concern's about that. Are the NIH and the Department of Energy working together to disseminate information on progress and findings?

Dr. **Watson**. DNA sequences are put together for distribution in an organization called Genbank, which is collaborative between the United States and Europe and Japan.

Mr. **Early**. Why is it stored if it is entered in three places?

Dr. **Watson**. The data is entered in many places. You can have it all on a compact disk, so storage is not a problem.

Mr. **Early**. Do you disseminate it to the scientific community?

Dr. **Watson**. Yes. Very important to the genome project is the National Center for Biotechnology Information.

Mr. **Early**. I would like you to expand on that for the record.

Dr. WATSON. Yes.

[The information follows:]

INFORMATION DISSEMINATION

The National Center for Human Genome Research (NCHGR) promotes rapid dissemination of genome research information starting with the researchers, who are encouraged to make their research findings available though public databases. To facilitate this process, NCHGR and the Department of Energy are jointly supporting the Genome Data Base (GDB) project at The Johns Hopkins University. This database collects human genome mapping data of all types. In addition, NCHGR supports the GBASE database at Jackson Laboratory, Bar Harbor, ME, which collects genome mapping data on the mouse. It is likely that genome database for one or two other imporant model organisms will be established during FY 1992. All these databases are easily accessible to researchers by either direct dial-up from a personal computer or terminal or, via the NSFNet, from any network-connected computer. For example, GDB has 5,000 registered users and is accessed an average of 2400 times per month with the average session time about 50 minutes. In addition, the databases produce off-line distributions on floppy diskette, magnetic tape, or CD ROM and in print, where appropriate. To facilitate international access, GDB has established, or is soon to establish, locally-funded satellite copies of the database in England, Germany, Sweden, Japan, and Australia.

Accurate, up-to-date databases of both DNA and protein sequence data are also important resources for the genome project. GenBank, the DNA sequence database, is currently operated under contract from the National Institute of General Medical Sciences (NIGMS) to IntelliGenetics, Inc., Mountain View, CA, and Los Alamos National Laboratory, Los Alamos, NM. This database will become an in-house project of the National Center for Biotechnology Information (NCBI), a division of the National Library of Medicine (NLM), in October 1992. As the amount of sequencing done by Human Genome Project (HGP) researchers increases, GenBank will become an increasingly important part of the HGP information dissemination infrastructure. NCHGR is, therefore, cooperating with NCBI to ensure that this database continues to meet the genome project's requirements for data dissemination. In addition, NCHGR is cooperating to establish a new database of expressed sequence tag (EST) sequenes within the NCBI.

COOPERATION WITH NLM

Mr. EARLY. What can you tell us about NCHGR cooperation with the National Library of Medicine?

Dr. WATSON. We have a very active relationship. They are located only two floors above us in the Lister Hill Center.

Mr. EARLY. Why don't you describe that for the record?

[The information follows:]

COOPERATION BETWEEN NLM AND NCHGR

NCHGR cooperates with the National Library of Medicine in a number of areas, especially with the National Center for Biotechnology Information. Since the NCBI is located just two floors above NCHGR in building 38A, communication is greatly facilitated. One area in which we cooperate is that of databases important to the Human Genome Project. One such database is GenBank, the DNA sequence database. This database will become an in-house project of the NCBI in October 1992. As the amount of sequencing done by Human Genome Project (HGP) researchers increases, GenBank will become an increasingly important part of the HGP information dissemination infrastructure. NCHGR is, therefore, cooperating with NCBI to ensure that this database continues to meet the genome project's requirements for data dissemination. In addition, NCHGR is cooperting to establish a new database of expressed sequence tag (EST) sequences within the NCBI.

Beyond these specific database projects, close collaborations between NCHGR and the National Library of Medicine have been benefical in numerous ways, among them:

NCBI computer scientists have provided initial technical advice to prospective NCHGR grant applicants in the area of genome databases, thus strengthening the technical plans presented in the grant applications.

Close collaboration between the extramural grants office of the NLM and NCHGR's Genome Informatics Program ensures that the respective interests of the two organizations are clearly defined and applications for projects in information dissemination and analysis appropriately assigned to either NLM or NCHGR. In areas of mutual interest, we try to assure that worthy projects are supported, to the maximum extent permitted by our combined budgets.

NCBI scientists have provided useful technical advice and recommendations regarding a wide range of projects related to genome information management. In particular, Dr. Lipman has participated in our meetings on numerous occasions and has made presentations to our Advisory Committee.

Dr. WATSON. I love to work with bright people.

Dr. David Lipman, who runs the National Center for Biotechology Information is extremely bright. I think he is doing a marvelous job in getting this information and putting it into a form which can be packaged for use by the outside world.

It is extremely important not only to get the information down but to make it accessible.

INTERNATIONAL COLLABORATION

Mr. EARLY. Some people believe that all of these costs should be shared; Japan should pay more as should the U.K. and France. Again, we want to be the leader.

Dr. WATSON. Besides the Genbank we have the Genome Data Base at Johns Hopkins. It was originally funded from the Howard Hughes Medical Institute.

Now it is funded from joint grants from the Department of Energy and NIH.

Mr. EARLY. Are they contributing anything toward it?

Dr. WATSON. Japan will pay some support, we think, in FY 1992, and certainly by the end of 1993, we should have a formal agreement.

EARLY DIAGNOSIS

Mr. EARLY. Doctor, they should have been sharing in these costs all the way.

I have some problems with some of the things that you said. When you spoke of breast cancer, you said that you will be able to tell a woman that she is at risk; know she is at risk. What are we going to do when we find out they are at risk?

Dr. WATSON. Have early and frequent mammography examinations. Right now the situation is that if your mother died at age 35 from breast cancer, you know it is very likely that the gene is in your family. That means that the genetic guess would be that you have one chance in two of also inheriting this gene.

Mr. EARLY. What are you telling me that I don't know?

Dr. WATSON. We can tell a woman that she is definitely not at genetic risk.

Mr. EARLY. There wont' be many. She is at less risk?

Dr. WATSON. Much less risk from genetic inheritance.

Mr. EARLY. On the Fragile X gene, you said they are retarded. I know the individual is retarded. If I am talking about a specific individual, you are telling me that you identified a gene and you can say now to John X, who is retarded, you identified the gene that John X is retarded. We know that. What are we going to do that is new, what are we going to be able to use that for?

Dr. WATSON. You can do conclusive diagnosis which you could not do before we found the gene. This is so new—I should say that this gene was found just six months ago.

There are a number of possibilities, we don't know enough yet. If you have one mentally retarded child, you do not know whether that is genetic or whether it has another non-genetic cause.

Mr. EARLY. I can appreciate that.

Dr. WATSON. With the genetic diagnosis you can say it is genetic. You can give the cause and say this is due to the gene that has been inherited through your mother.

Mr. EARLY. Doctor, in those charts you identified chromosome 17. Haven't we talked about that before, Dr. Healy? Is that associated with cystic fibrosis or Huntington's or one of these? What are you telling me that is different?

Dr. WATSON. Cystic fibrosis is located on chromosome 7 and Huntington's is on chromosome 4. There is no more important gene on the chromosome 17 than the breast cancer gene.

Dr. HEALY. A series of genes?

Dr. WATSON. There is a series, but we cannot say for sure whether there is one gene or a series of genes that are located at one point.

ELSI PROGRAM

Mr. EARLY. You have indicated that the cost of this has gone from 2 percent to, you say, 5.

You casually say it could approach 10. Ten percent is over $10,000,000. Why wouldn't that be equally shared by all countries, although the countries have different privacy and ethical standards.

Dr. WATSON. There are very practical aspects. Currently, we are spending more than $1,000,000, monitoring the testing for cystic fibrosis. Is it being done correctly? How are people using the information provided?

Mr. EARLY. Where are we spending that money? With you?

Dr. WATSON. Grants were made to seven different organizations. They are going to monitor whether these tests are useful and how the information is found.

The diagnostic tests cost money, so you don't just want to add another test to medical practices.

We are going to find many different genes, for each of which the ethical consequences are different.

Mr. EARLY. You said that you can never repair someone with genetic disorders.

Dr. WATSON. We cannot.

Mr. EARLY. You say never. Let's say you identify a problem in the brain with your imaging technique. You say there is the problem, and we have a drug that solves that problem. Don't we have the potential to do that genetically, too?

Dr. WATSON. The efforts to re-introduce genes back into people who have a problem gene are just starting. In NIH there is a new effort which is very exciting and which undoubtedly will lead to the curing of some diseases.

It may be possible to use gene therapy to cure all genetic diseases. I don't think you should count on this within the next 25 or 50 years.

Mr. **Early**. I don't have to worry about 25 to 50 years.

Dr. **Watson**. When I say never, it means not within my lifetime. But I think it would be cruel to tell a parent who has one mentally retarded child with Fragile X that we are going to be able to come up with a cure during the life of that child.

Mr. **Early**. That is conservative saying you don't want to tell them that. Don't you think you should provide a little light there. You cannot guarantee that you are not going to be able to do that.

Dr. **Watson**. I try to be optimistic but I don't want to be irresponsible.

BREAST CANCER—CHROMOSOME 17

Mr. **Early**. There are 24 chromosomes. Among these charts, I have one on 17. It shows chromosome 120. What is that?

Dr. **Watson**. That is 120,000 base pairs of genes known to be on the q arm of chromosome 1. The figure in the center of chart 1 is the chromosome. There are 24 different chromosomes. All of us have 46 chromosomes, 23 inherited from mother and 23 inherited from the father, and then you have the X and Y chromosomes.

TECHNOLOGY DEVELOPMENT AND INFORMATION DISSEMINATION

Mr. **Early**. With regard to the role of technology and the information dissemination, you are going to provide additional information for record for us as we requested?

Dr. **Watson**. Yes, sir, technology is very important. We have appointed Dr. Robert Strausberg to our staff. His major role is technology development and dissemination. He is a scientist and he is here in the back of the hearing room.

Our only problem is that he needs to visit these companies that are developing the technology and there are no travel funds available.

IMPACT OF TRAVEL REDUCTIONS

Mr. **Early**. Why don't you provide for the record what you are not going to be able to do because of lack of travel funds?

[The information follows:]

Travel Restrictions on Technology Transfer

Development of new technologies for chromosome mapping, sequencing, and information dissemination will be required in order to achieve goals of the Human Genome Program on schedule. Effective technology development and information dissemination for the Human Genome Program is best achieved through active collaborations between interdisciplinary teams of scientists including engineers, chemists, physicists, mathematicians, computer scientists and molecular biologists. In addition, it is vital that collaborations between academic and industrial scientists be encouraged and facilitated. These interactions will expedite the development of new technologies well-suited to the needs of genome researchers.

The NCHGR has actively encouraged such collaborations. This activity requires continual attention and nurturing to assure rapid progress. An important aspect of this NCHGR activity involves travel to academic and industrial laboratories. This mechanism allows NCHGR staff to directly monitor progress of ongoing technology development programs, to describe the needs of the genome program, to understand the technical capabilities and needs of the researchers, and to facilitate collaborations between scientists from diverse backgrounds.

Travel restrictions during FY 1992 have prevented the NCHGR from scheduling visits to industrial and academic laboratories including NIH funded genome centers, and have also limited our participation in scientific meetings which focus on technology development. NCHGR estimates that important opportunities for visits to approximately 15 companies and academic laboratories as well as participation in several scientific meetings have been missed because of the current restrictions on NIH travel. NCHGR staff opinion is that while the impact of these missed opportunities cannot be measured directly, it is significant.

Dr. WATSON. I wish we knew what we would find.

Mr. EARLY. As scientists, what opportunities will not be open to you if you don't have sufficient travel funds. You can do that for the record.

[The information follows:]

IMPACT OF FY 1992 TRAVEL REDUCTIONS

The National Center for Human Genome Research travel costs can be broken into site visit travel, advisory council/committee travel, travel for program coordination, travel to working group meetings, travel to chromosome workshops, and travel to other meetings.

Site visits are conducted both during the review of complex grant applications and after such grants are awarded. Complex, interdisciplinary applications can only be adequately evaluated on site, where the reviewers and NCHGR staff can talk to all the scientists, see demonstrations of their work, and evaluate the facilities. Reviews without site visits may lead to errors in evaluation which could be costly, if awards are not made to the best groups. The post-award site visits allow NCHGR staff to monitor the complex grants closely to assure that work is proceeding as planned and is coordinated with other grantees. The Program Advisory Committee strongly urged NCHGR to increase its efforts in this regard. Limitation of travel money has severely curtailed these activities. In 1992 NCHGR has reduced the number of site visits as well as the number of staff attending each, resulting in staff being significantly less well informed about how work is proceeding than we consider desirable.

National Advisory Council meetings are held three time a year to approve grant applications. The Program Advisory Committee meets twice each year to advise the NCHGR on where opportunities should be explored and to monitor progress of the program. With the limitation on travel funds, NCHGR has decided to postpone the September Council meeting and is canceling the June Program Advisory Committee meeting. These delays and cancellations will cause problems in awarding grants and assessment and management of the Human Genome Project.

Program coordination of the Human Genome Project both on a domestic and on an international basis is critical to the success of the Project. International coordination meetings are necessary both for the scientists participating in the Human Genome Project and for NCHGR staff in order to know what is occurring and what is planned in each country and to facilitate coordination and collaboration. It is not practical or reasonable to hold all such meetings in Washington as they involve people from around the world. NCHGR has had to curtail attendance at program coordination meetings held out of town. One meeting that NCHGR was unable to attend was the first meeting of the Japanese Ethical Working Group, which would have provided an opportunity for coordination with our ELSI program.

Working group meetings are held at the request of the Program Advisory Committee. These groups are organized along the scientific goals the NCHGR has established for the first 5 years of the Human Genome Project. These small groups are able to devote much more time and effort to evaluating progress and report back to the larger Program Advisory Committee so that appropriate policy can be developed. NCHGR has cut back the number of working group meetings in FY 1992 and has rescheduled others for a Washington metropolitan area location. It is difficult and also more expensive to have our advisors travel to Washington, D.C. for meetings rather than staff traveling to a more central location that minimizes time and expense for the group as a whole.

The chromosome workshops are a series of international annual meetings for each human chromosome that serve to coordinate activity among the researchers working on each chromosome. These meetings were started by NCHGR staff and have been adopted by the international genome community as a primary means of coordination. The majority of these meetings are domestic, with a few a year held abroad. Without staff attendance, we cannot assure that these meetings are carried out effectively, nor can we obtain the first-hand information on progress that is necessary for planning future activities. This year, NCHGR staff will not be able to attend as many of these meetings as would be desirable.

Other meetings NCHGR staff had planned were for the purpose of informing various groups about genome activities, especially in the area of ethical, legal and social implications and in technology transfer. Both of these areas are integral to the genome project and keys to successful accomplishment of the goals. Presentations by NCHGR staff had been planned for a number of major conferences, involving hundreds of people, and cancellation of these appearances has caused severe disruption for the planners of the conferences. For example, the Technology Development Specialist was unable to attend the Industrial Biotechnology Association annual meeting, which would have presented an excellent opportunity for communication with representatives of biotechnology companies about the objectives of the program and the opportunities for companies to participate in it and benefit from the research products.

Mr. NATCHER. Dr. Watson, we thank you and your associates for appearing before us at this time on behalf of your budget request for fiscal year 1993.

The Committee will now recess until 2:00 o'clock this afternoon.

[The following questions were submitted to be answered for the record:]

FUNDING BY GOAL

Mr. Natcher: Provide a breakout of 1991-1993 funding for genetic linkage maps, physical maps, DNA sequencing, informatics, new technology, and ethics.

Dr. Watson: The following table shows the breakout by category:

Category	FY 1991 Actual	FY 1992 Estimate	FY 1993 Estimate
Genetic Linkage Mapping	$13,799,000	$16,399,000	$17,271,000
Physical Mapping	23,229,000	27,531,000	28,994,000
DNA Sequencing	12,231,000	14,511,000	15,282,000
Informatics	9,000,000	10,734,000	11,305,000
New Technology	13,505,000	16,002,000	16,852,000
ELSI	3,989,000	4,970,000	5,234,000

The estimates for FY 1992 and FY 1993 are based on the same distribution as FY 1991. We do not expect major changes during this period.

EXPLORATORY GRANTS

Mr. Natcher: How many of your center grants are "exploratory"?

Dr. Watson: In FY 1991 one exploratory center was awarded. We anticipate awarding two new exploratory centers FY 1992 for a total of three centers in FY 1992 and FY 1993.

FUNDING HISTORY

Mr. Natcher: Provide a 1988-1993 funding table for the Center's activities, including the funds provided under the General Medical Sciences Institute in 1988-89.

Dr. Watson: The following table shows the funds provided by mechanism for FY 1988 through FY 1993.

FUNDING HISTORY
NATIONAL CENTER FOR HUMAN GENOME RESEARCH
(Dollars in thousands)

	FY 1988 1/ Actual		FY 1989 1/ Actual		FY 1990 Actual		FY 1991 Actual		FY 1992 Operating Level		FY 1993 President's Budget	
	No	Amount	No	Amount	No	Amount	No	Amount	No	Amount	No	Amount
Research Project Grants	63	16,767	102	26,709	132	41,645	174	54,652	181	60,876	201	66,158
Research Centers				300	4	8,320	9	20,787	12	27,234	12	27,234
Other Research	2	468	1	37	23	1,646	36	3,189	37	3,479	37	3,479
Total, Research Grants	65	17,235	103	27,046	159	51,611	219	78,628	230	91,589	250	96,871
					FTTP		FTTP		FTTP		FTTP	
Training					130	2,978	158	3,740	170	4,109	170	4,109
R&D Contracts				500	12	2,136	11	1,313	9	3,692	9	3,692
Res Mgmt and Support				684		2,802		3,708		5,488		5,757
Total, NCHGR		17,235		28,230		59,527		87,389		104,878		110,429

1/ Fiscal years 1988 and 1989 are shown for comparison purposes. Funds for this initiative were appropriated to the National Institute of General Medical Sciences. The Office of the Director, NIH supported the administrative costs associated with this initiative in FY 1989.

PUBLIC TELEVISION SERIES

Mr. Natcher: How much funding are you contributing to the public television series, "The Future of Medicine"?

Dr. Watson: The NCHGR provided $200,000 for "The Future of Medicine" public television series.

Mr. Natcher: How much of the series' funding is derived from other sources?

Dr. Watson: Additional funding of $2,350,000 has been provided from other sources for this series.

Mr. Natcher: Why did you decide the series would be an appropriate activity for the Center?

Dr. Watson: One of the Center's high priority goals in its Ethical, Legal and Social Implications Program, is public education about the practical implications of human genome research, which will take the form of new clinical tests and interventions. This series will illustrate and discuss the emerging role of genetic diagnostics in a wide range of medical settings, and has the potential to reach a broad public audience.

ADVISORY COUNCIL AND COMMITTEE

Mr. Natcher: What is the difference between the Program Advisory Committee and the Advisory Council?

Dr. Watson: The Program Advisory Committee on the Human Genome and the National Advisory Council for Human Genome Research both provide advice to the NCHGR. Each has very special functions and responsibilities and the input from both groups is vital to the NCHGR as it carries out its programs and formulates its plans for the future.

The Program Advisory Committee on the Human Genome advises the NIH on the best strategies for accomplishing the project. The Committee had a major role in the development of the Center's 5-year strategic plan. The Committee continues to identify new scientific opportunities and recommends initiatives that will promote the development of relevant new technologies. Finally, the Committee addresses the resource and training needs of the research community as they pertain to genomic analysis, as well as the implications of the Human Genome Program for individuals and society.

The National Advisory Council for Human Genome Research has the very specific function of reviewing research grant applications and recommending for approval those that show promise of making valuable contributions to the Human Genome Program. The Council is also charged with providing general advice to the NCHGR on both scientific and administrative issues.

The NCHGR makes every effort to keep each advisory body aware of the activities of the other, through the use of such mechanisms as reports at each meeting of activities of the other, and the exchange of minutes from each advisory body to the other. This coordination has served the NCHGR and its advisory bodies well and has enhanced our research program significantly.

STAFFING INCREASES

Mr. Natcher: When will your Center staff buildup be complete?

Dr. Watson: The Center has requested a modest increase of 6 FTEs for FY 1993, bringing our staffing level to a total of 51 FTEs. As our grant portfolio has expanded and programmatic growth has occurred in such areas as the Ethical, Legal and Social Implications Program, technology development, and informatics, additional staff is needed to carry out program development and monitoring of grant activities. Although the Center is small, we are required to carry out most of the functions of the large Institutes at NIH and to be responsive to the NIH, PHS, DHHS and the Congress. To fulfill this role, we have recently found it necessary to add additional staff in such areas as grants management, program planning and personnel administration.

As the program matures and we focus more specifically on accomplishing the goals of the Human Genome Project, increased monitoring and coordination by our staff will be needed. Therefore, I expect the number of FTEs will continue to increase at a moderate rate over the next few years.

SUCCESS RATE INCREASE

Mr. Natcher: Why is your research grant success rate projected to increase substantially from 1992 to 1993?

Dr. Watson: First let me say that the projection of success rate for NCHGR is very soft. It is based on models that NIH uses quite successfully to predict the number of applications and the size of the budgets requested, but which do not work well for NCHGR for two reasons. One reason is that our numbers are quite small and thus subject to statistical fluctuation. The second reason is that we have only a short history, shorter than needed to make the models valid. We simply cannot predict well how many applications we will get. Considering the momentum building in the genome program, we may well get more applications than predicted. There is an additional factor that makes the estimates uncertain, and that is that in FY 1993 the NCHGR will for the first time have a significant number of competing renewal grants. We do not have any experience to tell us how many of these will come in, how well they will do in peer review, or what budget level they will request. In most Institutes, competing renewal grants are significantly larger than new grants. Thus there are several reasons why the success rate may be overestimated. I believe the significant fact to look at is the total number of grants in each year. Because the President's budget allowed increases only in the RPG line, that line shows an increase of twenty grants for NCHGR, while all other budget categories show no increases, with the exception of a cost of living increase in Research Management and Support.

TOUR OF THE DIRECTOR

Mr. Natcher: How many days per week does the Director of the Center spend at the NIH campus? How many days per month does he travel on Center business?

Dr. Watson: I conduct a significant amount of Center business from my office in Cold Spring Harbor, New York, which is the arrangement made with the Director of NIH at the time I agreed to accept the appointment as Director of the National Center for Human Genome Research. The Deputy Director and staff of the Center consult with me by telephone, conference calls, FAX and express mail as the need arises. In this way, I keep abreast of developments on days I am not in Bethesda, Maryland. It is rare that a day goes by without some form of contact with Center staff.

In recent months, due to an extremely busy schedule, I have been able to spend only an average of about three days per month at the NIH campus. I do not feel the need to spend more time in Bethesda in order to provide the necessary leadership for the Center. I believe that the Deputy Director and other staff of the Center provide excellent coverage for me in my absence from Bethesda and frequent interaction with staff by phone and mail enables me to provide an appropriate level of policy guidance.

In addition to my time in Bethesda, I travel around the country and abroad for the Center, conducting meetings with grantees and other scientists, and making presentations on the Human Genome Project. As do many other ICD directors, I consider that being the spokesperson for the Center and the Human Genome Project is an important part of my job as Center Director. Because of the severe cut in the Center's travel budget, I have found it necessary to curtail much of my travel. Recently, I have restricted my travel to about 3 days per month. If additional travel funds were available, I would be travelling more on NCHGR business. In summary, I estimate I spend at least two days a week on genome business, which is the commitment I originally made.

FEASIBILITY RESEARCH

Mr. Natcher: You have described wanting to find "high risk, high payoff" research ideas. How will this sort of grant survive the competitive peer review process?

Dr. Watson: In 1990 the NCHGR developed a pilot project/feasibility program to specifically solicit applications that are in the "high risk, high payoff" category. There is one very important feature about this program that is critical to its success--an applicant does not need to have preliminary data, but does need to have a well thought out idea, a logical approach to the problem, and reasonable alternative approaches. Almost without exception, regular applications that do not include preliminary data receive poor priority scores during peer review. Applications for pilot projects are reviewed by the same study section that reviews regular investigator-initiated grants and have been well-received. The study section members were unanimously enthusiastic about this program during the review of the first set of applications and suggested to the NIH leadership that this program be adopted NIH-wide. Pilot project grants are awarded for a maximum of two years and are non-renewable. The maximum direct cost that can be requested is $100,000 per annum.

COMBINED BUDGET REQUEST-NIH AND DOE

Mr. Natcher: What is the total combined NIH and Energy Department budget request for the genome project?

Dr. Watson: The total request for the Human Genome Project in FY 1993 is $175,129,000. The National Center for Human Genome Research is requesting $110,429,000 and the Department of Energy's request is $64,700,000.

Mr. Natcher: Is the ratio between NIH and Energy funding the same as in previous years?

Dr. Watson: No. The following table represents the NCHGR share since the creation of the NCHGR.

	FY 1990 Actual	FY 1991 Actual	FY 1992 Estimate	FY 1993 Request
NCHGR	68%	65%	64%	63%

FIVE YEAR BUDGET PLAN

Mr. Natcher: Is your 1993 budget request consistent with the five-year cost plan you submitted to the committee last year?

Dr. Watson: The 1993 budget request is consistent with the five-year cost plan developed by NCHGR in terms of the general distribution among research areas and among budget mechanisms. However, the total amount requested is less than that estimated in the plan. The plan estimate for 1993 is $146 million as opposed to $110 million requested in the President's Budget.

DNA SEQUENCING GOALS

Mr. Natcher: What is the current cost of sequencing compared to a year ago? Is it likely that the cost will drop to 50 cents by 1995?

Dr. Watson: In 1990, the cost of sequencing performed by highly skilled researchers in laboratories devoted to DNA sequencing was estimated to be about $2 to $5 per finished base. These costs must be reduced to below 50 cents per base pair before large-scale sequencing will be cost-effective.

The NCHGR is administering an ambitious research program to support DNA sequencing technology development. The largest investment so far has been in feasibility studies for large-scale sequencing with associated technology development. These grants were awarded as a result of a special solicitation for studies using advanced state-of-the-art DNA sequencing technology to accomplish large-scale sequencing projects at a higher rate and lower cost than is currently possible. In the initial phases, research performed through these grants has already generated interesting results. For example, in the first year of their grant, Drs. Robert Waterston, Washington University, St. Louis, and John Sulston, Medical Research Council, England, have sequenced 220,000 base pairs of C. elegans and are ahead of schedule toward their goal of 3 million base pairs in 3 years. Importantly, Dr. Waterston estimates that scale-up of his current technology would permit sequence determination at about $1 per base pair. Further refinements of sequencing strategy, methodology, and computational analysis are expected to further reduce this cost.

Therefore, during this year significant improvements in the cost of DNA sequencing have been reported and with further refinements it is reasonable to expect that the cost will drop to about fifty cents per base pair in 1995.

SEQUENCING TECHNOLOGY

Mr. Natcher: How much will you spend to develop new sequencing technologies in 1992 and 1993?

Dr. Watson: During FY 1991 the NCHGR allocated about $12.3 million for DNA sequencing technology development. The largest investment, about $10 million, was made to support feasibility studies for large-scale sequencing with associated technology development. In addition, the NCHGR supported studies for significant improvements of current gel-based sequencing technology and for development of entirely new approaches to DNA sequencing, with the potential for order of magnitude improvements in the rate and cost of sequencing.

In FY 1992 the NCHGR issued a Request for Applications for New DNA Sequencing Technology in Support of the Human Genome Program. Using funds specifically appropriated for DNA sequencing, the NCHGR will support an increased number of regular research project grants and developmental grants which are designed to encourage feasibility studies of highly innovative approaches to DNA sequence analysis. The NCHGR budget for DNA sequencing technology development for FY 1992 is estimated to be $14.5 million, and for FY 1993 is anticipated to be $15.3 million.

LINKAGE MAPPING GOALS

Mr. Natcher: Do you still expect to complete all linkage maps by the end of 1993?

Dr. Watson: The linkage mapping program of the NCHGR comprises two components. I expect that the first of these, the "framework" or "index marker" maps, will be completed by the end of 1993. The framework maps consist of especially useful markers, but are of lower resolution--less detailed--than the maps called for in the 5-year plan. We have emphasized the development of the framework maps on a very short time scale for two reasons: they will expedite the construction of the higher resolution--more detailed--linkage maps and they will be extremely useful to investigators in the larger scientific community who are working to map and isolate disease genes and genes that determine other important traits.

I expect that the second component of the NCHGR linkage mapping program, the high resolution maps, will be completed by the end of 1995, as called for in the 5-year plan.

PHYSICAL MAPPING GOALS

Mr. Natcher: Will physical mapping be completed within your five-year target?

Dr. Watson: I am confident that the U.S. Human Genome Program will meet the goals for physical mapping that are set out in the 5-year plan. Progress in this area has been very rapid in the past few years. For example, the human genome research center at Washington University in St. Louis is working to construct the physical map of the human X chromosome. This group, headed by Dr. David Schlessinger, has already completed a physical map of a portion of the X chromosome, which is as large as some of the smaller human chromosomes. Finally, there is currently enough mapping activity on certain chromosomes, such as chromosomes 17, 21, Y and X, that we expect the physical maps of those chromosomes to be completed within one to two years. When the efforts in the U.S. and abroad are considered together, it is likely that useful physical maps for all human chromosomes will be available to the scientific community by the end of 1995.

RESEARCH CENTERS

Mr. Natcher: How are the Department of Energy centers different from yours?

Dr. Watson: In both the NIH and DOE programs the centers are the keystone of the mapping effort. There are similarities in the centers programs but also many differences. The DOE centers have very similar goals to those of some of the NIH centers, i.e., to map an entire human chromosome and develop new technology. However, each center is employing somewhat different mapping strategies. It is important at this stage of the project to have several large groups using different strategies in order find one strategy that is successful. The NIH centers program is broader than the DOE program, since some of the NIH centers are studying the genomes of model organisms and others are emphasizing medical aspects of human genome mapping. Finally, the DOE centers are considerably larger than the NIH centers in terms of budget and personnel.

Mr. Natcher: Do you expect any growth in the number of centers beyond the current twelve?

Dr. Watson: By the end of FY 1992, NCHGR expects to have established eight Human Genome Research Centers, one Biotechnology Center, and three exploratory centers. So far, the existing human genome research centers have been extremely important and have made significant contributions to the NCHGR mission. There are still opportunities in genome research that can best be realized by establishing additional large interdisciplinary research groups. I hope that we will be able to capitalize on these opportunities in the future.

MISSION OF THE HUMAN GENOME PROJECT

Mr. Natcher: We have heard criticism that a substantial share of genome funding is allocated for projects and activities that are not directly related to your primary mission. How do you respond to this, Doctor?

Dr. Watson: We are surprised to hear that there is criticism of this type. In our opinion, and that of our advisors, all the research and other activities we support is directly related to achieving the goals of the human genome program. The 5-year plan developed by us at the beginning of the program has been well accepted and is being followed very closely. In addition to research that falls strictly under the definition of mapping and sequencing, we support a number of activities that are necessary to the accomplishment of mapping and sequencing goals. One is technology development. In this area, only projects that can be clearly seen to enhance mapping and sequencing activities are considered.

Another area is informatics. Here again, we support the development of tools that help the mapping and sequencing effort and allow the information generated to be organized, stored and distributed to users. Getting the results of the genome project out to users has been an integral part of the Human Genome Initiative from the beginning and we consider it our responsibility to make sure it happens. For the same reason, we encourage our major projects to have outreach components. These are designed to assure that research results and technology get out to the scientific and medical community in the most efficient manner. Unfortunately, this does not happen automatically, because there are costs involved, as well as commitment of people and equipment.

We also support training of investigators to increase the number of scientists who can participate in genome research as well as to enable other scientists to acquire knowledge about genomic technology, so that they can use it in their research.

Of course, there is also the Ethical, Legal, and Social Implications Program, which we consider an essential element of the human genome project. The purpose of this program is to ensure that the information we generate is used for the benefit of individuals and society, and not misused.

I want to stress that every award we make is scrutinized by the Initial Review Groups, our National Advisory Council and the Program Advisory Committee, for relevance to the goals of the programs. We consider it essential to remain focussed on our goals, in order to assure that we reach them.

GENOME INFORMATICS TECHNOLOGY

Mr. Natcher: Is current computer technology adequate to handle the large volume of information that will be produced by the genome project?

Dr. Watson: Although the genome project is handling very large amounts of data, compared to traditional biological research projects, the total amount of data is modest when compared to that routinely handled in high-energy physics experiments, atmospheric modelling projects, or even by large automated teller machine systems. Therefore, we are able to use off-the-shelf computing hardware for both laboratory data management and public databases. While customized software must be developed, especially for laboratory data management and data analysis, current software and database engineering methods and technologies can support the systems needed. The real shortage we face is in the number of qualified computing professionals who have expertise in the kinds of data management and analysis problems posed by the genome project.

CO-FUNDING WITH DEPARTMENT OF ENERGY

Mr. Natcher: Do you co-fund any genome projects with the Department of Energy besides the Genome Data Base?

Dr. Watson: As a general rule, it is more convenient to make separate awards to the same investigator, rather than to co-fund in the technical sense, i.e., make one award to which both agencies contribute. In this broader sense, a number of investigators receive funding from both NCHGR and DOE for different aspects of their overall genome research programs. For example, the genome centers at the University of Utah and at the Baylor College of Medicine are both supported by core center grants from the NCHGR. This mechanism provides funding for shared research resources and facilities at institutions where there already is a significant amount of ongoing and closely related, independently funded genome research. At both the Utah and Baylor centers, some of the independently funded grants have been awarded by the Department of Energy human genome program. Thus, the very active mapping and technology development efforts at both of these centers receive both NIH and DOE support.

NCHGR and DOE also have a standing agreement about joint funding of chromosome mapping workshops and other genome conferences. The agencies generally share the costs of these meetings on an equal basis.

Finally, in the Ethical, Legal, and Social Implications Program, a number of projects have been co-funded, in the strict sense, with the DOE because of shared programmatic interest.

GENOME DATA BASE

Mr. Natcher: How much international funding do you hope to obtain for the Genome Data Base?

Dr. Watson: Last summer we initiated talks with representatives of the genome programs of all countries with organized genome projects, with the aim of generating substantial support for Genome Data Base (GDB) from them. The interest among foreign governments in contributing support to make this a project of international scope and importance has been very strong. To date we have organized two meetings attended by officials from the genome programs in Belgium, Canada, Denmark, France, the United Kingdom, Austria, the Netherlands, Italy, Sweden, Japan, Switzerland, and the European Community. In addition, we have recently received expressions of interest from Germany. We expect the database to receive funds from the United Kingdom and Japan in FY 1992 and from the European Community, France, and the Nordic Council in FY 1993. Other countries can be expected to make smaller commitments within the next year to eighteen months. At this time no firm specific commitments have been made, but it is our hope that international funding will constitute about half of the cost of GDB within 2-3 years.

Mr. Natcher: How does the [Genome] Data Base differ from GenBank at the Library of Medicine?

Dr. Watson: The Genome Data Base (GDB) and GenBank differ primarily in terms of their content, the kinds of scientific data they collect. The GDB, operated by the Welch Medical Library of The Johns Hopkins University collects human genome mapping data of all types. Mapping data indicates the location of a gene or other "marker" on a chromosome. In addition to the mapping data for individual genes and markers, GDB contains information on several kinds of chromosome maps, including genetic linkage maps--obtained by analyzing the inheritance of genetic traits or markers; physical maps--obtained, for example, by constructing maps of overlapping pieces of cloned DNA from a chromosome; and cytogenetic maps--obtained by observing chromosomes through the microscope. GDB contains very limited information on DNA sequences, but where the sequence of a gene has been determined, GDB contains instructions on how to obtain the sequence from the GenBank database.

GenBank contains information related to the sequence of nucleotides making up the genes and genomes of both the human and more than a thousand other organisms. This database is currently operated under contract from NIGMS to IntelliGenetics, Inc., Mountain View, CA, and Los Alamos National Laboratory, Los Alamos, NM, and is planned to become an in-house project of the National Center for Biotechnology Information, NLM, in October 1992. GenBank contains very minimal information on the map locations of the sequences it represents. For human genes, the map location information in GenBank is derived from GDB.

Since the human genome project aims ultimately to map and sequence the human genome, the results of the project will appear in both these databases. Therefore, close coordination between the databases will be required. At present the bulk of genome research is directed toward mapping and technology development, so most of the data generated by genome researchers goes into GDB. As the maps are completed and the focus of the project shifts to sequencing, the bulk of new data generated will then go into GenBank.

INTERNATIONAL FUNDING

Mr. Natcher: How much funding does your Center award to scientists outside the United States?

Dr. Watson: In the 5-year plan, the NIH and DOE stated that the Human Genome Program "is not limited to the United States...[and]...that there are many opportunities where international collaboration could enhance progress." Accordingly, we "have a policy of welcoming international collaboration in the basic research aspects of the Human Genome Project. Because it is desirable to encourage other countries to contribute financially to this project, the agencies have decided that they will, in general, not fund a foreign research project unless it will make a unique contribution that cannot be readily duplicated in the United States. The agencies will, however, fund joint research projects between the United States and another country if there is also joint funding from the other country."

In accordance with this policy, the NCHGR does not currently support any foreign grants, but does contribute to two international collaborations. The first is a pilot effort to determine the sequence of the DNA of the roundworm Caenorhabditis elegans. This work is being carried out by Dr. Robert Waterston at the Washington University in St. Louis, in collaboration with Dr. John Sulston at the Laboratory of Molecular Biology in Cambridge, England, whose work is supported by the Medical Research Council of the United Kingdom. In the course of this work, a small proportion of the U.S. funds are actually spent in Cambridge.

This project is, at present, the most advanced of the several preliminary efforts in large-scale sequencing supported by the NCHGR. In its first year, over 220,000 base pairs of DNA sequence were determined, which was approximately 10 percent ahead of schedule. At the same time, the cost of the sequencing was reduced to an estimated $1.00 per base pair. As this research project proceeds, the investigators anticipate a significant increase in the rate of sequencing and a concomitant decrease in the unit cost.

The second collaboration involves a series of small, international workshops on the maps of individual human chromosomes. These workshops provide an opportunity, usually on an annual basis, for the international community of scientists working on the genetic and physical maps of each chromosome--typically between 25 and 100 investigators--to exchange data, develop collaborations, and construct state-of-the-art consensus maps which are distributed to the entire scientific community. The support of these workshops is shared by funding agencies from a number of countries. The workshop sites are usually at, or near, major laboratories or centers working on the chromosome of interest. Approximately half of the 1992 workshops will be in the U.S. Each agency provides travel support for its own nationals and the host country provides the rest of the meeting costs.

ETHICAL, LEGAL, AND SOCIAL IMPLICATIONS PROGRAM

Mr. Obey: The National Center for Human Genome Research provided the Committee with its first year "report card" to demonstrate progress made toward mapping the human genome. I find it disappointing that the report card failed to include an important component, that of measuring the success of developing policy recommendations for addressing important legal, social and ethical questions. Is there a good reason for not including a timeframe for setting goals for each year of the project in the area of ethical, legal and societal issues?

Dr. Watson: The NCHGR's chromosome-based "Report Card" does not provide an appropriate format for illustrating our progress in the Ethical, Legal and Social Implications (ELSI) Program, because the problems being addressed in that program are not peculiar to any particular human chromosome. However, the ELSI Program does have a yearly workplan for approaching its five year goal of providing policy options on the issues it has identified as highest priority during this period. This workplan is follows.

ELSI PROGRAM WORKPLAN AND INTERIM GOALS

FY 1990

1. Develop ELSI agenda and establish extramural grants program (full Program Announcement published January 1990)

2. Launch series of outreach conferences to broaden program participation and refine agenda.
   (10 conferences held across U.S. in 1990-91, all producing subsequent research project applications and agenda-setting reports.)

3. Identify highest priority policy needs to address in first five years.
   (CACR submitted in January 1991 identifying 3 high priority areas: a) clinical integration of new genetic tests; b) fairness in use of genetic information by insurers and employers; c) privacy of genetic information.

FY 1991

1. Launch special initiatives to address three highest priority areas:

   A. Clinical Introduction of New Genetic Tests
   (a. NAS/IOM study of professional policy options in the clinical integration of new genetic tests initiated, October 1990.
   b. NIH consortium of clinical studies on the introduction of cystic fibrosis carrier testing initiated, September 1991.)

   B. Fairness in Genetic Information Use
   (a. NIH-DOE Task Force on Genetic Testing and Insurance initiated, May 1991.

b. NIH-DOE ELSI Working Group analysis of draft Americans with Disabilities Act regulations submitted to EEOC, April 1991)

C. Privacy of Genetic Information
(a. NIH-DOE consortium of grantees addressing privacy issues established, September 1991)

2. Identify highest priority educational needs to address in first five years

(a. NCHGR Education workshop held identifying public participation and professional training as major needs, March 1991.
b. NIH Science Education Partnership Awards co-sponsored by NCHGR, September 1991.)

FY 1992

1. Develop consent and confidentiality guidelines for genetic research involving large families.
(a. NIH-sponsored AAAS workshop held, outlining issues for follow up by NCHGR and NIH Office of Protection from Research Risk staff, March 1992.)

2. Initiate clinical studies of genetic risk assessment for multifactorial disorders
(a. NCHGR-NCI collaboration on clinical use of genetic cancer risk markers initiated, December 1991
b. NCHGR-NHLBI collaboration on clinical use of genetic cardiovascular disease risk markers initiated, January 1992.)

3. Convene NIH-DOE ELSI Grantees for mid-course status report on extramural research and education efforts.
(planned for September 14-16, 1992.)

4. Sponsor pilot public forum series on ELSI issues.
(Knoxville, TN (October 1991); Iowa City, IA (April 1992); Blacksburg, VA (April 1992); Washington DC (September 1992))

FY 1993

1. Disseminate initial reports on three high priority issue areas:

A. NAS/IOM report on the clinical integration of new genetic tests (due May 1993)

B. NIH-DOE Insurance Task Force report (due May 1993)

C. NIH-DOE Genetic Privacy collaboration report (due May 1993)

2. Commission "Core Concepts" studies of initial reports as basis of five year plan report

3. Launch national public participation and professional education initiative through extramural grant-making program.

FY 1994

1. Disseminate professional practice recommendations from clinical studies of single gene (cystic fibrosis) and multifactorial genetic testing and counseling.
2. Implement national public participation and professional education initiative.
3. Develop plans for insuring systematic local integration of ethical, legal and social considerations into ongoing policy-making in genetics (e.g., regional ELSI centers), through extramural grant-making program.

FY 1995

1. Convene NIH-DOE ELSI grantees for status report on five year goals.
2. Produce and disseminate final comprehensive report on ELSI policy options.
3. Establish second five year plan for program, focussed on facilitating the discussion and implementation of informed professional and public policy options.

Mr Obey: You mention in the FY 93 budget justification that we can expect a final report outlining policy options on genetic testing and insurance. Will this report include recommendations from the Administration?

Dr. Watson: The NIH-DOE ELSI Working Group's Task Force on Genetic Testing and Insurance will deliver its final report on policy options in May 1993. This task force is composed of NIH and DOE grantees examining insurance-related issues, insurance industry policy analysts, consumer group representatives and experts in health policy serving as consultants. Its report will be delivered to the NIH and DOE, to Congress, to the insurance industry and to state governments simultaneously. Any appropriate Administration recommendations for policy-making would follow as a response to the findings of this report.

Mr. Obey: When can the Committee expect to receive a comprehensive report describing the policy options to address legal, ethical and societal issues which are raised by the Human Genome Project?

Dr. Watson: One of the five year goals established for the ELSI Program in the first five year plan for the U.S. human genome project is to "identify and define the major issues and develop initial policy options to address them." While reports addressing subsets of the program's agenda will be produced along the way (as the program timeline indicates) a comprehensive report on the highest priority issues is thus scheduled to be available by the end of FY 1995.

ETHICAL, LEGAL, AND SOCIAL IMPLICATION PROGRAM

Mr. Stokes: A second issue involves transferring these new testing options to health professionals. The fear is that without proper guidance, the widespread clinical introduction of these new tests could lead to their misapplication and misinterpretation by professionals and patients alike. What are some of the challenges in this area?

Dr. Watson: Integrating new genetic tests into clinical practice in ways that avoid their misapplication and misinterpretation by professionals and patients poses three sets of challenges which the NCHGR is helping to address: 1) developing the clinical protocols and professional practices that should guide the conduct of testing in the clinical setting; 2) communicating those guidelines to the health professions; and 3) informing patients and the public about the benefits and limits of new tests as they emerge.

Currently, the NCHGR's efforts to address these challenges are focused on the most prominent example of a new genetic test that has potential for widespread use, the test for the major DNA mutations causing cystic fibrosis (CF). Explaining the implications of CF mutation testing to individuals and families is a sensitive, complex and time-consuming process for genetic professionals. Increasingly, individuals without known family histories of CF are becoming interested in this form of reproductive risk assessment, and asking their health professionals about this test.

In order to help health professionals know how best to respond to requests for such services, NCHGR is coordinating a consortium of seven research projects, aimed at defining the best methods for educating and counseling individuals who want to be tested for CF mutations. The results of these studies will be communicated directly to the relevant health professional communities through their professional societies and other influential scientific organizations like the National Academy of Sciences/Institute of Medicine.

These results will also be integrated into ongoing NCHGR-supported programs of public and professional education, such as the high school teacher training programs being developed by the major genome research centers, to help foster a "genetically literate" population of health care consumers.

COST OF SEQUENCING

Mr. Stokes: I addressed the issue of the cost of sequencing last year, in questions I submitted to the Center. Where are we in the development of technology which will provide increased translation, and decreased costs in sequencing?

Dr. Watson: The NCHGR is supporting a series of feasibility studies for large-scale sequencing, with associated technology development. In the most advanced project, Drs. Robert Waterston, Washington University, St. Louis, and John Sulston, Medical

Research Council, England, have already sequenced 220,000 base pairs of C. elegans, ahead of their own schedule. Dr. Waterston estimates that scale-up of his current technology would allow sequencing at about $1 per base pair. Further refinements are expected to further reduce this cost to $0.50 per base pair in the near future.

In addition, the NCHGR is also supporting other investigator-initiated research projects aimed toward improving gel-based DNA sequencing technology. For example, NCHGR supported researchers are attempting to improve DNA sequencing in several ways, such as:

- improved phage and plasmid vectors
- automation of DNA sequencing reactions
- rapid separation of sequencing reaction products by capillary and thin gel electrophoresis
- new approaches for increasing the information content of sequencing gels
- analysis of sequencing reactions by mass spectrometry

Each of these approaches has the potential to reduce the cost and increase the rate of DNA sequence analysis, and when used in combination, can make an even greater impact on technology improvement. For example, NCHGR grantee Dr. Lloyd Smith, University of Wisconsin, has developed a new instrument with a throughput of 8,000 bases per hour, nearly ten times faster than currently available technology.

The NCHGR is also sponsoring research projects designed to develop entirely new approaches to DNA sequence analysis. These are high risk, high payoff projects which could make order of magnitude improvements in the cost and rate of sequencing. For example, NCHGR grantees Dr. Christopher Becker, SRI International, and Robert Levis, Wayne State University, are developing DNA sequencing methodologies based on mass spectrometry, and Dr. Edward Cox, Princeton University, is developing DNA sequencing methodology based on atomic force and scanning tunneling microscopies.

In response to Congressional appropriation language, the NCHGR issued a Request for Applications for New DNA Sequencing Technology in Support of the Human Genome Program. Using funds appropriated for this purpose the NCHGR will support an increased number of regular research project grants and developmental grants which are designed to encourage feasibility studies of highly innovative approaches to DNA sequence analysis.

DATA PROCESSING AND ANALYSIS

Mr. Stokes: Do you have a better sense than you did last year as to how much of your budget is being used for the development of technology?

Dr. Watson: During FY 1991, the NCHGR allocated about $13.5 million for technology development. In addition, many of the major mapping and sequencing projects supported by NCHGR include technology development as an integral part of the mapping and sequencing activity, but the costs cannot readily be separated.

Mr. Stokes: It is my understanding that the handling and analysis of the raw sequence data as they are read directly from the sequencing gel is limited for large-scale sequencing projects. To what extent has DNA sequencing technology changed in the last 10 or so years? What are some of the new developments in this area?

Dr. Watson: Research efforts in the area of DNA sequencing technology development have made significant advances during the past decade. Improvements have been made in three general areas including:

- cloning and preparation of DNA for sequence analysis
- separation of DNA sequencing reaction products
- reading and interpretation of the raw DNA sequence data.

In each of these areas technological advances have been significant. Especially important for increased rate and decreased cost of sequencing is the increasing use of automation. For example, automated systems have been developed for:

- preparation of DNA sequencing templates
- running the sequencing gels
- reading the raw sequencing data
- assembling the data into long contiguous DNA sequences
- interpreting the sequence information.

In addition, continued development of sequencing approaches, tools and methods compatible with automation is ongoing. Examples of NCHGR-supported DNA sequencing technology development to improve current gel based methods include the following:

- Drs. Jen-i Mao, Collaborative Research Incorporated, and Robert Weiss, University of Utah, are testing a new method termed multiplexing which has the potential to generate significantly more information per sequencing gel

- Dr. Thomas Brennan, Genomyx, Inc., is developing a new sequencing instrument that incorporates mass spectrometry for sample detection

- Dr. Lloyd Smith, University of Wisconsin, is developing a new sequencing machine incorporating ultrathin gel electrophoresis.

These and other approaches supported by NCHGR have the potential to lead to continued improvement of DNA sequencing technology.

MINORITY PARTICIPATION

Mr. Stokes: The justification and statement indicate that a planning grant was recently awarded to investigators at Howard University College of Medicine who wish to establish cell collections from African American families for genetic studies. The justification also indicates that existing collections contain samples mostly from caucasians. How much was provided for this grant?

Dr. Watson: This is a two year planning grant. The total cost of this two-year program, which began in FY 1991, is approximately $430,000.

Mr. Stokes: Up to this point, to what extent have minority samples been collected?

Dr. Watson; Although we do not have exact numbers, we do know that there are a few scientists working on individual projects in which samples from minorities are collected. These samples are collected from families exhibiting certain diseases which are of special interest to those individual investigators. The resource that is proposed by the Howard University group will be available to the scientific community for general studies, such as looking for the frequency of various markers in different populations. For example, it is known that the different mutations that cause cystic fibrosis occur with different frequencies in people from northern Europe as opposed to southern Europe.

Mr. Stokes: Considering the disproportionate incidence of disease and chronic illness in the African American community, why has the Center not done more in this area?

Dr. Watson: I am not aware of any evidence that genetic-based diseases affect African Americans more than any other ethnic group. While many diseases and illnesses may have a genetic basis, it is probably the non-genetic factors, such as nutrition, life-style, and environment, that result in increased morbidity and mortality in African Americans. The mission of the Center is not to study specific diseases, but to support the development of valuable resources, rapidly ,and efficiently, so that they can then be used by biomedical scientists who are studying specific diseases. For the purpose of creating the basic maps and the DNA sequence of human genome, it is irrelevant whether the genomes studied are African-American, since the genetic information is known to be extremely similar. These resources can be used to help understand the biological basis of the disease, to develop effective therapies, and to diagnose diseases regardless of the racial or ethnic origin of the people affected by the disease.

Mr. Stokes: How many projects have been funded in the last two years? How many are currently being funded? What total level of funding has been provided?

Dr. Watson: The NCHGR supports minority activities through various mechanisms, i.e., research supplements, minority travel awards, or minority pre-doctoral fellowship awards. The NCHGR supported 12 minority individuals in FY 1991 and estimates support of 16 minority individuals in FY 1992. The request for FY 1993 includes the support of 17 minority individuals. The total funding for these three years is $1,743.

MINORITY EFFORTS

Mr. Stokes: How many and what percentage of employees of your institute are minorities? Please provide a breakdown by race and grade level. How many are employed in a research capacity? What recruitment and promotion activities are being supported?

Dr. Watson: Forty-two percent of the NCHGR staff, or 18 out of a total of 43 employees, are under-represented minorities. The breakdown by grade level is as follows: GS 1 through 8, 61% of the employees in this group are minorities; GS 9 through 12, 63% are minorities; and GM 13 through 15, 14% are minorities. A racial profile of the Center includes 16 blacks, 1 Hispanic, and 1 Asian. Black women serve as Chief of the Research Grants Branch and as Chief of the Grants/Contracts Management Section. Since the NCHGR has no intramural program, none of our employees is engaged in the conduct of research. Our scientific staff are engaged in program development and the management and monitoring of extramural research grants.

Since its inception, the Center has participated in a Federal Equal Opportunity Recruitment Program (FEORP) plan established by the Office of the Director, NIH. This plan was established to ensure that selecting officials give adequate consideration to the promotion and recruitment of minority candidates in special target occupations. The Center has made significant progress in fulfilling its FEORP goals.

In addition to the FEORP program, the Center has made considerable efforts to recruit under-represented minorities to our staff. Our scientific staff have contacted the NIH Associate Director for Minority Programs and have solicited minority institutions for minority candidates to serve as scientist/administrators on our staff. So far, we have found very few candidates with appropriate scientific backgrounds. Currently, we have two vacancies for scientist/administrators. Supervisory staff have been instructed to make special efforts to recruit minority candidates for these positions.

In addition, within the Center, there have been several promotions for minorities. Two minority women have been promoted from clerical positions to positions with career ladders to the GS-12 level. Another minority female is being mentored in the Grants Management Office, for a possible professional position as a Grants Management Specialist. Also, at the present time we have on board a minority female in a temporary position with intent to place this person in a permanent position, when one becomes available.

Mr. Stokes: Please describe for the committee the resources and funding levels which will be provided for minority-specific research activities in FY 1993. How do these levels compare to last year's levels? Total funding represents what percentage of your budget?

Dr. Watson: The following table represents NCHGR support for minority programs.

National Center for Human Genome Research

Minority Programs
(Dollars in thousands)

	FY 1991 Actual No.	FY 1991 Actual Amt.	FY 1992 Estimate No.	FY 1992 Estimate Amt.	FY 1993 Request No.	FY 1993 Request Amt.
Research Supplements for Minority Undergraduates	1	3	1	32	2	68
Research Supplements for Minority Graduate Res. Ass't	1	8	1	37	1	39
Research Supplements for Minority Investigators	1	230	2	396	2	396
National Minority Pre-doctoral NRSA Program	6	154	6	160	6	160
Minority Travel Awards	3	10	6	25	6	25
Total	12	405	16	650	17	688
Percentage of Extramural Funding		.46%		.62%		.62%

Mr. Stokes: To what extent are you working with the Office of Minority Health to effectuate these goals?

Dr. Watson: In developing the NCHGR's plan to increase the participation of under-represented minorities in the Human Genome Program, we had discussions with the Associate Director for Minority Programs, and many of his suggestions were incorporated into our plan. As an example, one of his models for increasing participation, and collaborations between faculty and students in minority and majority institutions, has proved very successful. Over the past year, the institutions in the Baltimore area have developed such a collaboration and are planning to request funds to provide a research experience at Johns Hopkins University this summer for minority students. The lack of travel funds has prevented us from replicating this model in other cities, like Houston, New York, Detroit, St. Louis and San Diego.

The NCHGR is working on a continuing basis with the Office of Minority Health. The Office has established a Minority Health Roundtable, to function as an in-house body to foster the exchange of ideas on how the Office of Minority Health can fulfill its mandate. An NCHGR staff member has been asked to participate as a member of this group. Through our participation in the Roundtable, we will not only contribute to the discussions, but will have the opportunity to capitalize on ideas generated by the Office of Minority Health and other members of the Roundtable.

NIH STRATEGIC PLAN

Mr. Pursell: Where does the NCHGR fit into the NIH strategic Plan?

Dr. Watson: The NCHGR fits into the NIH framework for a strategic plan extremely well, and under many, if not most, of the scientific initiatives described in that plan. Genetics, both from the point of view of basic mechanisms and in relation to the role of genes in various diseases, is a theme that runs throughout the draft strategic plan, just as it does throughout the research programs that NIH supports. The role of the Human Genome Project in facilitating these various high priority areas is, therefore, significant. The scientific initiatives in the framework where the research supported by the NCHGR features most prominently, are Molecular Medicine and Biotechnology.

INTERNATIONAL SUPPORT

Mr. Pursell: How much international support is there for research into the human genome? Please quantify, by country, the specific monetary contribution.

Dr. Watson: The Human Genome Program is an international research program, in which several other industrialized nations are actively participating. Funding agencies in France, Japan, the United Kingdom, and Italy, as well as the European Community, are all providing significant support for research that is identified as genome research. Several other countries, including Sweden, Denmark, Germany, Russia, and the Netherlands, are contributing to the Human Genome Program to a smaller degree. An estimate of world-wide expenditure in the leading countries for FY 1992 is approximately $225,000,000, as shown in the following tables. The U.S. is contributing about 73 per cent of the total, a proportion that has steadily decreased from about 80 per cent in FY 1988.

The estimate of foreign investment in the Human Genome Program is very rough for several reasons, including the fact that the several national programs have different scientific scopes. Furthermore, the foreign contributions recorded should be considered as underestimates, because those programs do not generally include salary expenses in their reports; in the U.S., personnel support accounts for 60 to 70 per cent of the budget.

INTERNATIONAL FUNDING FOR HUMAN GENOME RESEARCH
(U.S. dollar equivalent in millions)

	1988 est.	1989 est.	1990 est.	1991 est.	1992 est.
United States	$27.9	$46.7	$87.4	$135.1	$163.9
European Community (EC)			9.8	9.8	11.8
France				9.0	18.0
Italy	1.2	1.2	1.2	2.1	2.1
Japan		6.2	8.8	16.5	21.7
United Kingdom	____	3.7	3.7	3.7	7.9
Estimated total	$29.1	$57.8	$110.9	$176.2	$225.4

Footnote: For the foreign programs, these represent estimates only. Budgets continue to change due to political decisions. Exchange rates also fluctuate. Different countries have different fiscal years, which overlap only partially. We have not attempted to divide the budgets of all countries into a comparable fiscal year period. For comparison purposes, two important points need to be taken into account. First, salary and other overhead costs, which represent a significant portion of the costs of the NIH genome program, are generally not included in the international budgets. Second, each of the above programs has different definitions for "genome research", which also complicates an easy comparison of international funding. Most of these programs do not include support for research on the genomes of model organisms, which is a significant component of the NCHGR program. On the other hand, some of these programs include classical human genetics research and research on genetic diseases, which are not specifically included in the NCHGR program. Several other countries that are not listed, also contribute to the Human Genome Project, but to a smaller degree. This includes Sweden, Denmark, Germany, the former Soviet Union and the Netherlands. In addition, UNESCO and NATO have made some contributions.

INTERNATIONAL FUNDING FOR HUMAN GENOME RESEARCH
(in local currency)

	1988 est.	1989 est.	1990 est.	1991 est.	1992 est.
United States In Millions dollars	$27.9	$46.7	$87.4	$135.1	$163.9
European Community 1/ In Millions ₠ (15.6 Mio ₠ 90-92)			7.8₠	7.8₠	9.4₠
France 2/ In Millions ₣ (150M ₣ 88-90)				50.0₣	100.0₣
Italy 3/ In Billions £ (6 billion £ 87-90) (12.5 billion £ 91-95)	1.5£	1.5£	1.5£	2.5£	2.5£
Japan 4/ In Millions ¥		800¥	1,128¥	2,114¥	2,780¥
United Kingdom 5/ In Millions £ (6.3 M £ 89-91/92) (4.5 M £ 92/1993)		2.1£	2.1£	2.1£	4.5£

1/ - Comm of European Communities, Human Genome Analysis (1990-1992), Information Package Update (1-16-92) from Bronwen Loder, Consultant, EC Human Genome Project

2/ - Human Genome News, January 1991

3/ - State Department document, American Embassy Rome 11-5-90

4/ - Nature. V 340; 31 August 1989; Nature V 351;20 June 1991; Nature V 353; 12 September 1991 Science and Technology Agency letter 11-20-91, State Department document, American Embassy Japan January 1991

5/ - G-nome News, Number 5, Winter 1991; G-nome News, Number 7, Summer 1991

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Center for Human Genome Research

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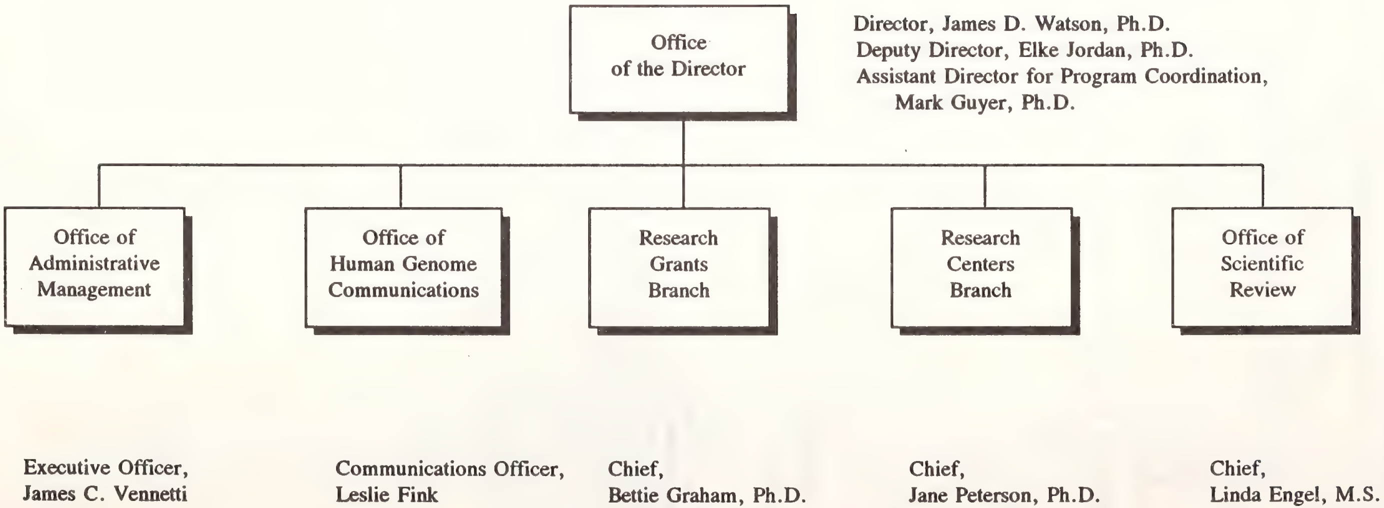
NATIONAL INSTITUTES OF HEALTH
NATIONAL CENTER
FOR HUMAN GENOME RESEARCH

ORGANIZATION STRUCTURE



NATIONAL INSTITUTES OF HEALTH

National Center for Human Genome Research

For carrying out section 301 and Title IV of the Public Health Service Act with respect to human genome research, [$105,261,000] *$110,429,000*: *Provided*, That of the funds made available under this heading, [$10,000,000] *$10,965,000* shall not become available for obligation until September 30, [1992] *1993*.

(Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 1992.)

NATIONAL INSTITUTES OF HEALTH

National Center For Human Genome Research

Amounts Available for Obligation 1/

	1991 Actual	1992 Appropriation	1993 Estimate
Appropriation..................	$89,731,000	$105,261,000	$110,429,000
Sequester order................	-1,000	---	---
Section 514 (a) reduction.......	-150,000	---	---
Section 514 (b) reduction.......	-2,163,000	---	---
Section 214 travel reduction....	---	-29,000	---
Section 513 (a) travel reduction	---	-47,000	---
Section 513 (a) S & E reduction.	---	-307,000	---
Subtotal, adjusted appropriation..............	87,417,000	104,878,000	110,429,000
Real transfer to: Other accounts for Shannon Awards...............	-19,000	---	---
Subtotal, adjusted budget authority...........	87,398,000	104,878,000	110,429,000
Unobligated balance lapsing.....................	-9,000	---	---
Total obligations..........	87,389,000	104,878,000	110,429,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: FY 1991 - $150,000; FY 1992 - $150,000; FY 1993 - $150,000.

NATIONAL INSTITUTES OF HEALTH

National Center for Human Genome Research

Budget Mechanism
(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	No.	Amount	No.	Amount	No.	Amount
Research grants:						
Research projects:						
Noncompeting	99	$32,500	138	$47,428	110	$36,776
Admin. supplementals	(2)	659	(4)	414	(4)	429
Competing:						
Renewal	9	5,255	16	5,967	34	13,317
New	62	14,848	25	6,332	53	14,093
Supplements	4	1,390	2	735	4	1,543
Subtotal, competing	75	21,493	43	13,034	91	28,953
Subtotal, res. proj	174	54,652	181	60,876	201	66,158
Research centers:						
Specialized/comp. centers	9	20,787	12	27,234	12	27,234
Other research:						
Research career programs	4	249	8	540	8	540
Other research related	32	2,940	29	2,939	29	2,939
Subtotal, other research	36	3,189	37	3,479	37	3,479
Total, research grants	219	78,628	230	91,589	250	96,871

Training:						
Individual awards:						
Noncompeting..................	5	160	16	421	17	447
Competing:						
New..........................	15	397	7	194	6	168
Subtotal, individual.............	20	557	23	615	23	615
Institutional awards:						
Noncompeting..................	129	2,952	141	3,352	147	3,494
Competing:						
New..........................	9	231	6	142	---	---
Subtotal, institutional..........	138	3,183	147	3,494	147	3,494
Total, training..................	158	3,740	170	4,109	170	4,109
Research and development contracts	11	1,313	9	3,692	9	3,692
Research management and	FTEs		FTEs		FTEs	
support..........................	37	3,717	45	5,488	51	5,757
Total..........................	37	87,398	45	104,878	51	110,429

NATIONAL INSTITUTES OF HEALTH

National Center for Human Genome Research

CROSSWALK - 1991 Actual

(Dollars in thousands)

PROGRAM ACTIVITY	MECHANISM Research Grants Research Projects	 Research Centers	 Other Research	 Training Programs Individual	 Institutional	 Research and Development Contracts	 Research Management and Support	 Total
Human genome research...........	$54,652	$20,787	$3,189	$557	$3,183	$1,313		$83,681
Research management and support........							$3,717	3,717
Total..........	54,652	20,787	3,189	557	3,183	1,313	3,717	87,398

NATIONAL INSTITUTES OF HEALTH

National Center for Human Genome Research

CROSSWALK - 1992 Appropriation

(Dollars in thousands)

	MECHANISM							
	Research Grants			Training Programs				
PROGRAM ACTIVITY	Research Projects	Research Centers	Other Research	Individual	Institutional	Research and Development Contracts	Research Management and Support	Total
Human genome research...........	$60,876	$27,234	$3,479	$615	$3,494	$3,692		$99,390
Research management and support........							$5,488	5,488
Total..........	60,876	27,234	3,479	615	3,494	3,692	5,488	104,878

NATIONAL INSTITUTES OF HEALTH

National Center for Human Genome Research

CROSSWALK - 1993 Estimate

(Dollars in thousands)

MECHANISM

PROGRAM ACTIVITY	Research Grants			Training Programs		Research and Development Contracts	Research Management and Support	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional			
Human genome research...........	$66,158	$27,234	$3,479	$615	$3,494	$3,692		$104,672
Research management and support........							$5,757	5,757
Total..........	66,158	27,234	3,479	615	3,494	3,692	5,757	110,429

NATIONAL INSTITUTES OF HEALTH

National Center for Human Genome Research

Summary of Changes

1992 Estimated budget authority	$104,878,000
1993 Estimated budget authority	110,429,000
Net change	+5,551,000

	1992 Current Estimate Base		Change from Base	
	Pos. (FTE)	Budget Authority	Pos. (FTE)	Budget Authority
CHANGES:				
A. Built-in:				
1. Within grade increases		$2,652,000		+$30,000
2. Annualization of January 1992 pay raise		2,652,000		+22,000
3. One less day of pay		2,652,000		-10,000
4. January 1993 pay raise		2,652,000		+75,000
5. Increased cost of centrally furnished services		476,000		+289,000
6. DHHS Working Capital Fund		57,000		+2,000
7. Increased cost of service and supply fund		278,000		+15,000
8. Increased cost of supplies and materials		2,783,000		+78,000
Subtotal				+501,000
B. Program:	No.	Amount	No.	Amount
1. Research project grants:				
a. Noncompeting	138	$47,428,000	-28	-10,652,000
b. Admin Supplements	(4)	414,000		+15,000
c. Competing	43	13,034,000	+48	+15,919,000
Total	181	60,876,000	+20	+5,282,000
2. Research management and support:	FTE		FTE	
a. Additional FTE	45	$5,488,000	+6	+246,000
b. Program decrease				-478,000
Subtotal				+5,050,000
Total changes				+5,551,000

NATIONAL INSTITUTES OF HEALTH

National Center for Human Genome Research

Budget Authority by Activity
(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	FTEs	Amount	FTEs	Amount	FTEs	Amount
Human genome research....	---	$83,681	---	$99,390	---	$104,672
Research management and support............	37	3,708	45	5,488	51	5,757
Total Obligations......	37	87,389	45	104,878	51	110,429
Unobligated balance lapsing................		9		---		---
Total, budget authority..	37	87,398	45	104,878	51	110,429

NATIONAL INSTITUTES OF HEALTH

National Center for Human Genome Research

Budget Authority by Object

	1992 Appropriation	1993 Estimate	Increase or Decrease
Total number of full-time permanent positions	50	55	+5
Total compensable work years:			
Full-time equivalent employment	46	52	+6
Full-time equivalent of overtime and holiday hours	1	1	--
Average ES salary	$103,666	$106,543	+$2,877
Average GM/GS grade	10.1	10.1	---
Average GM/GS salary	43,872	45,495	+1,623
Average salary, grades established by act of July 1, 1944 (42 U.S.C. 207)	55,152	57,193	+2,041
Personnel compensation:			
Full-time permanent	$1,985,000	$2,254,000	+269,000
Other than full-time permanent	201,000	228,000	+27,000
Other personnel compensation	43,000	49,000	+6,000
Total, personnel compensation	2,229,000	2,531,000	+302,000
Personnel benefits	421,000	474,000	+53,000
Benefits for former personnel	2,000	2,000	---
Travel and transportation of persons	99,000	135,000	+36,000
Transportation of things	15,000	16,000	+1,000
Rent, communications, and utilities	48,000	50,000	+2,000
Printing and reproduction	62,000	64,000	+2,000

	1992 Appropriation	1993 Estimate	Increase or Decrease
Other services:			
Project contracts	3,692,000	3,692,000	---
Centrally furnished services	476,000	782,000	+306,000
Other	1,785,000	1,339,000	-446,000
Supplies and materials	49,000	51,000	+2,000
Equipment	302,000	313,000	+11,000
Grants, subsidies & contributions	95,698,000	100,980,000	+5,282,000
Total	104,878,000	110,429,000	+5,551,000

NATIONAL INSTITUTES OF HEALTH
National Center for Human Genome Research

Significant Items in Senate Appropriations Committee Report

Funding for DNA Sequencing

The Senate in its report 102-104, page 139, stated, "...The Committee believes that the HGP [Human Genome Project] will bring untold health benefits to humankind but is not satisfied that NIH and NCHGR has fully explored ways of accelerating the project. To achieve this objective the cost of DNA sequencing must be substantially reduced and secondly the rate at which DNA sequencing can be done must be increased. The Committee has included an increase of $2,000,000 to more fully focus on these two vital steps to reduce the overall time that the project will take. The Committee requests a report by the end of January on the efforts to meet this objective and prospects for doing so."

Action taken or to be taken - A report on NCHGR DNA sequencing efforts has been prepared and submitted to the Senate. A request for applications to develop improved sequencing technology was issued on December 20, 1991.

NATIONAL INSTITUTES OF HEALTH

National Center for Human Genome Research

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1992 Amount Authorized	1992 Appropriation	1993 Amount Authorized	1993 Budget Request
Research and Investigation......	Section 301	42§241	Indefinite	$100,769,000	Indefinite	$106,320,000
National Research Service Awards	Section 487(d)	42§288	Authorizing legislation is pending	1/ 4,109,000	Authorizing legislation is pending	1/ 4,109,000
Total Budget Authority........				104,878,000		110,429,000

1/ This training authority is shared with other research training programs of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration.

NATIONAL INSTITUTES OF HEALTH

National Center for Human Genome Research

Appropriation History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1990	$100,000,000	$62,000,000	---[1]	$59,938,000
1990 Sequester				-400,000
1991	108,029,000	66,131,000	108,264,000	87,418,000[2]
1991 Sequester				-1,000
1992	110,487,000	93,115,000	109,309,000	104,878,000[3]
1993	110,429,000			

[1] The Senate did not provide funds for the National Center for Human Genome Research; however, the Senate allowance included $61,847,000 for the Human Genome Initiative within the National Institute of General Medical Sciences' account.

[2] Excludes enacted administrative reductions of $2,313,000.

[3] Excludes enacted administrative reductions of $383,000.

Justification

National Center for Human Genome Research

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite.

Budget Authority:

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
37	$87,398,000	45	$104,878,000	51	$110,429,000	+6	+$5,551,000

General Statement

The Human Genome Project is a world-wide initiative to identify the full set of genetic instructions contained inside human cells and to read the complete text encoded in human DNA. The U.S. effort is administered by the National Center for Human Genome Research (NCHGR), within the National Institutes of Health, in partnership with the Department of Energy. The Human Genome Project will provide powerful tools to help scientists clear the research hurdles that now keep them from understanding the molecular essence of inherited diseases or susceptibility to diseases, such as cancer, arthritis schizophrenia, alcoholism, Alzheimer's disease, and manic depression.

The potential benefits of the Human Genome Project are manifold and include prevention and therapy of many diseases. The fuller understanding of human molecular genetics will result in better prevention strategies for some diseases which, in turn, will reduce illness and suffering, and lower health care costs. One such prevention strategy could be the modification of an individual's lifestyle to avoid risk factors, based on an understanding of disease processes and the individual's genetic susceptibilities. Similarly, improved prenatal screening will allow parents to make better choices for their children's pre and post-natal care, leading to healthier children. The improved understanding of the genetics of the human immune system, particularly the genetics of an individuals' ability to respond to foreign substances such as bacteria or viruses, will allow the design of better approaches to vaccination against or immunotreatment of a wide variety of diseases.

In terms of improved treatment, technologies based on human genome research will give rise to a number of new products in addition to the obvious use of gene therapy or other approaches to correction of the genetic defect. These include new DNA-based diagnostic tests and a variety of new instruments for research and clinical laboratories, such as a new generation of automated DNA sequencers. A number of new therapeutics can be expected, in conjunction with advances in the area of structural biology, based on the specific structure of genes or gene products. Information about genetically determined responses and reactions to specific drugs will allow the development of custom pharmaceuticals targeted to specific genetically defined sub-populations.

The Human Genome Project includes several distinct but interrelated research efforts: genetic linkage mapping, physical mapping, DNA sequencing, informatics, technology development and transfer, and the ethical, legal and social implications of the project. To identify initial goals and monitor research in these areas, a scientific plan was developed for the first 5 years of the Human Genome Project. A companion budget plan was also prepared. The present budget request is for the third year of the first 5-year period.

Overview of Research Activities

Genetic linkage maps are based on the way genetic markers, including genetic diseases, are inherited in families. By studying how frequently two markers are inherited together over several generations, scientists can determine the order of the genes on a chromosome and approximate their location. Gene identification research projects are currently limited by the poor quality and nonuniform distribution of markers on today's genetic maps. In FY 1991, the NCHGR awarded several research grants to support the development of a "framework linkage map" for each human chromosome consisting of approximately 300 evenly spaced "index" markers of very high quality. The construction of these maps is slated for completion by the end of FY 1993. The maps will provide a series of highly informative landmarks that can be used to rapidly localize each new marker to a particular interval on a chromosome.

Physical maps give the actual physical distances--number of DNA nucleotide bases--between genes on a chromosome and also allow scientists to get access to the DNA in a particular region of the genome. There are many different types of physical maps, each of which is at a different level of resolution. One important type of physical map consists of a set of overlapping pieces of cloned DNA which completely spans an entire chromosome.

In recent years, physical maps have played a key role in the isolation of the genes involved in a number of interesting and important genetic diseases, including the genes for the *Fragile X Syndrome*, which is the cause of the most common form of inherited mental retardation among males; for *Familial Adenomatous Polyposis (FAP)*, an inherited form of colon cancer; for *Charcot-Marie-Tooth Syndrome*, a degenerative disorder of the peripheral nervous system that leads to muscular atrophy; and for *Kallman Syndrome*, which leads to an unusual cluster of abnormalities, including a loss of the sense of smell and failure of the testes to develop properly. The search for each of these genes was greatly aided by the products of the Human Genome Project.

DNA sequencing is the process of determining the order of the nucleotide bases in DNA. The genetic information a gene carries is contained in the order of nucleotides in that gene's DNA. To understand how genes work, scientists must be able to read and interpret this DNA language. At present, DNA sequencing is too costly to consider sequencing large regions of human DNA. Under NCHGR support, several large-scale pilot DNA sequencing projects have been initiated to try to reduce the cost significantly by improving current technology and/or by developing new approaches to DNA sequencing. Among these are projects devoted to sequencing the DNA of a bacterium, *E. coli*, and a round worm *C. elegans*. The 5-year goal for DNA sequencing is to improve current methods and/or develop new methods for DNA sequencing that will allow large-scale sequencing of DNA at a cost of $0.50 per base pair.

Informatics. Both databases and tools for analyzing data will be produced by the Human Genome Project. Databases will provide scientists with easy access to available research information about the human genome and genomes of other organisms. During FY 1991, the NCHGR and the Department of Energy co-funded the Genome Data Base project at Johns Hopkins University. International participation in the support and oversight of this vital resource is expected for subsequent fiscal years. This database will collect, edit, and distribute human gene mapping data and several types of maps in support of genetic and other biomedical research.

New technology is needed to speed up and simplify both chromosome mapping and DNA sequencing while improving the accuracy and reliability of results. In the area of DNA sequencing, the NCHGR has initiated an ambitious program of support of research projects designed to develop entirely new approaches to DNA sequence determination. It is hoped that these high-risk, high-payoff projects will lead to order-of-magnitude improvements in the cost and rate of DNA sequencing. To accelerate progress in this area further, the NCHGR has recently issued a Request for Proposals (RFA) entitled "New DNA sequencing technology in support of the Human Genome Program." The RFA is designed to encourage applications from scientists who have not traditionally requested research support from the NCHGR or NIH but who are interested in testing new and conceptually creative ideas for large-scale DNA sequencing.

The ethical, legal and social implications of human genetics research are wide-ranging. An ethics working group helps to plan and coordinate this part of the Human Genome Project. Three major areas have been identified for initial study: privacy of genetic information, fairness in the use of genetic information in employment and insurance, and safe use of genetic information in clinical practice. The research tools generated by the Human Genome Project will speed up the process by which genetic testing capabilities become available for clinical use. The newly developed genetic test for cystic fibrosis provides a good model for developing and testing the best approach to the use of genetic tests in general medical practice. For this reason, the NCHGR, working with other NIH Institutes, has embarked on a 3-year research initiative to define the best methods for educating and counseling individuals who want to be tested for CF mutations.

The National Center for Human Genome Research was established in FY 1990. Prior to this, funding for the Human Genome Project at NIH was appropriated to the National Institute of General Medical Sciences in FY 1988 and FY 1989. The table below lists funding appropriated to the NCHGR.

Year	Amount	FTE
FY 1990	$59,538,000	26
FY 1991	87,398,000	37
FY 1992	104,878,000	45

Purpose and Method of Operations

To reach the goals outlined in its first 5-year research plan, the NCHGR uses the full-range of funding mechanisms, including research project grants, program project grants, center grants, conference grants, fellowships, training grants and research and development contracts. Each activity supported by the NCHGR is reviewed by program staff to determine the most appropriate funding mechanism. All applications receive two-tier peer review according to standard NIH procedures.

Research project grants are used to fund investigator-initiated proposals, submitted either unsolicited or in response to specific Requests for Applications announced by the Center. The NCHGR awards research project grants to stimulate and test new ideas, to develop new technologies, and to allow smaller institutions and laboratories the opportunity to participate in the Human Genome Project in a meaningful way.

Research center grants are a major component of the Human Genome Program at NIH. These awards go to multi-disciplinary centers comprised of interdisciplinary groups of scientists tackling major objectives of the program. The centers serve as resources to other genome researchers for both research materials and research techniques. Each center has an active outreach program, including, an informatics component to assure that genomic information is well organized and easily accessible to all researchers, and efforts to inform the medical community and to educate the public.

Research career awards are emphasized by NCHGR. Because of the need for individuals with skills in interdisciplinary research, NCHGR is encouraging investigators in other scientific disciplines to take advantage of the opportunity to train in genomic research. A Special Emphasis Research Career Award has been announced to support training activities and research projects for individuals under the supervision of advisors who have distinguished themselves in the area of genomic research.

Conference grants are important to the genome project for bringing together scientists in specialized areas to rapidly exchange ideas and materials, share information and reach consensus on the state of various maps.

Training awards are used to bring scientists into genome research. New investigators will be needed to develop, use and apply the knowledge gained by the Human Genome Project. Interdisciplinary pre-doctoral training and specialized post-doctoral training are offered as well as training for more senior scientists who want to change the direction of their research.

Research and development contracts are used by the NCHGR to support the acquisition of resources such as cell lines, DNA probes or data for use by genome researchers. Additionally, the NCHGR uses inter-agency agreements with other Federal agencies for a variety of tasks of joint interest to NCHGR and those agencies. Frequently this is more efficient and avoids two agencies duplicating an effort.

The Program Advisory Committee on the Human Genome provides advice and guidance in pursuit of the goals of the Human Genome Project. A joint NIH-DOE sub-committee, composed of members of the Program Advisory Committee on the Human Genome and the DOE Health and Environmental Research Advisory Committee, monitors and coordinates the human genome programs at the two agencies. The 5-year research plan was developed by these advisory committees and forms the basis for new initiatives and funding plans.

On occasion, the advisory groups establish NIH-DOE joint working groups to report back to the parent committees on different aspects of the human genome program. Currently, the areas being addressed by working groups are: mapping, sequencing, informatics, the mouse as a model organism, and the ethical, legal, and social implications of genome research.

Overall Budget Policy

The FY 1993 budget request for the National Center for Human Genome Research is $110,429,000. This amount represents an increase of $5,551,000 or 5.29 percent over the comparable 1992 estimate. The research supported by the NCHGR is entirely basic research.

The FY 1993 budget request for research project grants is $66,158,000. This level will support 110 non-competing grants at an average cost of $334,000 and 91 competing grants at an average cost of $318,000, a 4.97 percent increase over the FY 1992 average cost for competing research grants. The total number of research project grants is 201, an increase of 20 grants and $5,282,000 over the FY 1992 estimate.

The FY 1993 budget request for research centers is $27,234,000. This level will support the same number of research centers at the same level as in the FY 1992 estimate.

The FY 1993 budget requests $3,479,000 for other research grants. This level will support 8 research career awards and 29 other research-related awards. This represents the same number and dollar level as in the FY 1992 estimate.

The FY 1993 budget requests $4,109,000 for research training awards. This level will support 23 individual fellows and 147 full-time trainee positions under institutional training awards, for a total of 170 trainees. This is the same as the FY 1992 estimate.

Nine research and development contracts and inter-agency agreements are anticipated to be made during FY 1993 at a level of $3,692,000.

The FY 1993 budget request provides $5,757,000 for research management and support activities, an increase of $269,000, 4.9 percent, over the comparable FY 1992 estimate. This increase will provide for pay-related and other inflationary increases.

National Center for Human Genome Research

Human Genome Research

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1993 Authorization: Indefinite

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$83,681,000	$99,390,000	$104,672,000	+$5,282,000

The Human Genome Project is the most important biological mapping expedition ever imagined. Scientists are working together to develop a variety of biological maps that, taken together, will enable a broad range of researchers to pinpoint specific genes on human chromosomes and understand their function and control. The most detailed map, the DNA sequence itself, will help scientists to decipher the genetic instructions encoded in the estimated 3 billion pairs of nucleotide bases that make up human DNA. Analysis of this information will lead to new strategies to diagnose, treat, and possibly prevent human disease.

Most inherited diseases are rare, but taken together, there are more than 3,000 disorders known to result from single altered genes. Many other diseases, although not inherited (passed from one generation to the next), are genetic in that they are caused by alterations in the DNA of somatic (body) cells during the lifetime of the individual. Researchers have learned that isolating and understanding the structure of a gene and the molecular alteration, or mutation that results in disease is a crucial first step in developing a solution to disease. Progress in understanding the causes of cancer, for example, took a leap forward when cancer genes were discovered.

Gene mutations also play a role in many of today's most common diseases, such as heart disease, diabetes, immune system disorders, and birth defects. These diseases are believed to result from complex interactions between genes and environmental factors. When genes that predispose individuals to particular diseases have been identified, scientists can study how specific environmental factors, such as food, drugs or pollutants interact with those genes and their products to cause disease. Such understanding can then be used to design preventive or therapeutic measures.

Funding for the human genome research activity was appropriated to the National Institutes of General Medical Sciences in FY 1988 and FY 1989.

Funding appropriated for this activity to the National Center for Human Genome Research is as follows:

Year	Amount
FY 1990	$56,727,000
FY 1991	83,681,000
FY 1992	99,390,000

Rational for the Budget Request

The FY 1993 budget request for the human genome research activity is $104,672,000, an increase of 5.3 percent over the FY 1992 estimate of $99,390,000. The following are highlights of research activities funded in this program.

Genetic Linkage Mapping

As defined in the NIH-DOE 5-year plan, the goal is the development of genetic linkage maps of human chromosomes, such that approximately 1,500 easy-to-use markers are uniformly arrayed along all chromosomes. Existing linkage maps are characterized by the relatively poor quality of the markers and their nonuniform distribution. This limits their usefulness in gene identification projects.

Framework Linkage Maps

In FY 1991, as a first step towards attaining this genetic mapping goal, the NCHGR awarded several research grants to support the development of a "framework linkage map" for each human chromosome. The complete framework map will consist of approximately 300 "index" markers of very high quality. These framework maps will provide a series of highly informative landmarks that can be used to rapidly localize any new gene or other marker to a particular interval. The framework maps will be immediately useful to scientists looking for specific genes, such as those associated with particular diseases or syndromes. In the first year of the framework map project, about 300 markers were identified as being index marker candidates. These markers are publicly available through a catalogue which is being widely distributed. During FY 1992, these markers, along with newly isolated ones, will be evaluated for their ease of use and evenness of distribution along the chromosomes.

The Next Step

During FY 1993, the framework linkage mapping project will be completed; research will then be directed toward filling in the map with more closely-spaced markers to the level established in the 5-year plan. Prior to FY 1993, high resolution mapping projects have been initiated for a limited number of human chromosomes (1, 3, 4, 5, 17, 21, 22, X). Efforts will be expanded during FY 1993 to improve mapping technology and to map the remaining chromosomes.

Physical Mapping

Yeast Artificial Chromosomes (YAC)

New mapping tools known as YAC's--Yeast Artificial Chromosomes--were first introduced about 5 years ago. However, it was not until recently that their utility for cloning DNA, especially fragments of complex DNA such as that of the human, was proven and their usefulness for the development of a high resolution physical maps demonstrated. Using YAC vectors, physical maps have been constructed of the genomes of the fruit fly, *D. melanogaster*, and the round worm, C. *elegans*, and long-range maps of the human genome are beginning to materialize.

With respect to physical maps of human DNA, the most significant progress has been made by Dr. David Schlessinger and colleagues at Washington University in St. Louis, who have used YACs to construct a physical map of the tip of the long arm of the human X chromosome. The region of the X chromosome which has been mapped in this way is 50 million bases in size. This represents 1.5 percent of the human genome and is, in fact, equivalent in size to one of the smaller human chromosomes, such as chromosome 21 or 22. Using a number of techniques, a large number of YAC clones were isolated from this region of X and assembled into contigs (overlapping, ordered clones of DNA) which were up to 8 million bases in length. It is important to note that this exceeds one of the criteria established in the 5-year plan, which called for maps consisting of contigs at least 2 million base pairs long.

Fragile X Syndrome

Fragile X Syndrome is the most common form of inherited mental retardation in males. It occurs in 1 in 1,000 males and 1 in 2,500 females. An international effort, in which U.S. scientists played a vital role, has now isolated the defective gene. The search for the gene causing the Fragile X Syndrome illustrates how the resources developed by the Human Genome Project facilitated the international search for this gene.

First Dr. Stephen T. Warren, of Emory University School of Medicine in Atlanta, Georgia, developed essential cell lines from Fragile X patients which were used to localize the affected gene to a region of the X chromosome. Next, investigators at Baylor College of Medicine and Washington University in St. Louis and scientists in the United Kingdom, isolated YAC clones containing the regions of the human X chromosome that span the Fragile X site. A group of U.S. scientists, in collaboration with scientists from Western Europe and Australia, then sequenced the genomic region containing the Fragile X site and identified the mutation that causes the disease. All the participating groups of U.S. scientists received some of their support from the NCHGR. In addition to finding the genetic basis for this important form of mental retardation, these findings demonstrated a new mode through which genetic defects arise. In the case of the Fragile X Syndrome, the genetic defect is caused by abnormal duplication of part of the gene. These results have already been very useful, as they have enabled the development of a quick and specific diagnostic test for Fragile X Syndrome.

Research into Improving YACs

As described above, the development of Yeast Artificial Chromosomes (YACs) that carry from 200,000 to 750,000 base pairs of DNA, has made it possible to assemble overlapping cloned DNA over large contiguous regions of the human genome. However, as scientists have gained more experience with the existing YAC systems, it has become apparent that there are some problems yet to be solved. For instance, a large number of YACs in the earliest collections--possibly as many as 40 percent--carry two pieces of unrelated human DNA rather than one large contiguous piece. Of course, this type of artifact causes significant problems when scientists try to determine what piece of DNA in the genome lies next to that cloned in a given YAC. In FY 1993, additional effort will be directed to studying factors that lead to this type of rearrangement of DNA in YACs and how to prevent it.

Mapping More Chromosomes

NCHGR is currently supporting physical mapping activity on more than half of the 23 human chromosomes. However, the 5-year goal for physical mapping, to assemble 2 million base pair contigs covering most of the chromosomes, still poses a significant challenge. The mapping of the 50 million base pair region on the X chromosome took several years to complete. Thus, in order to accomplish the 5-year goal, additional research is needed to develop more efficient ways to assemble physical maps.

Physical mapping efforts on additional chromosomes are needed. These will serve to test the utility of different strategies and technologies. The involvement of new groups in the project is an important avenue for bringing new ideas and technology to bear on this difficult problem. Funding of research on physical maps of additional chromosomes will not only increase the coverage of the entire genome, but also accelerate the development of new technology.

Sequencing Technology

The NCHGR is supporting two approaches to the goal of reducing sequencing costs to a level that is acceptable for sequencing the entire human genome. First, it can be anticipated that considerable improvements will result from economies of scale. Currently available sequencing techniques and strategies have never been tested on a scale large enough to determine if economies can be obtained that will significantly reduce the cost. A second approach is to support entirely new, innovative technologies.

Novel Sequencing Technology

The NCHGR has initiated an ambitious program to develop entirely new approaches to DNA sequence analysis that promise to be cheaper and faster than current methods. Among the new approaches being pursued are that of Dr. Christopher Becker at SRI International, who is testing the application of time-of-flight mass spectrometry to DNA sequence analysis, and that of Dr. Edward Cox at Princeton University who is developing DNA sequencing technology based on atomic force and scanning tunneling microscopies. More work in this area is needed and an expansion of activities is planned for FY 1993.

Large-scale sequencing efforts

The NCHGR has also initiated a number of pilot large-scale sequencing efforts to test the capabilities of current DNA sequencing techniques. Each of these pilot projects is being done with DNA of particularly high biological interest.

One team of investigators, headed by Dr. Robert Waterston at Washington University, St. Louis and Dr. John Sulston at the Medical Research Council, England, are performing a 3-year feasibility study to sequence 3 million base pairs of the roundworm *C. elegans*, an important model organism for the study of developmental biology. In the first year of their grant, these researchers have already sequenced 220,000 base pairs and are ahead of their own schedule. Dr. Waterston estimates that scale-up of their current technology would permit sequence determination at close to one dollar per base pair. He now anticipates that the entire sequence of *C. elegans*, estimated to be 100 million base pairs, could be completed this decade if appropriate funding is available. This effort represents an outstanding opportunity to develop technology that is robust and cost-effective enough for large-scale sequencing of human DNA.

Dr. Frederick Blattner, at the University of Wisconsin, has undertaken an ambitious project to sequence the entire genome of the bacterium *Escherichia coli*, which is over 4 million base pairs. This organism has for many years been the subject of intense study by geneticists and biochemists. By starting with well-established DNA sequencing technology, Dr. Blattner set up a pilot scale "production line" and is automating many of the steps.

Dr. Blattner has recently completed a contiguous 91,000 base pair sequence and identified 85 potential genes, of which 57 may represent genes not previously identified. These results support the notion that the most practical and efficient approach for identifying all possible genes and regulatory regions will be complete genomic sequencing.

Dr. Leroy Hood at the California Institute of Technology in Pasadena, California is studying the organization and function of a large group of genes involved in the mammalian immune response by sequencing a region of human DNA containing the genes for T-cell receptors and the homologous region of mouse DNA. Through a comparative study of these loci, Dr. Hood expects to identify, and elucidate the role of, conserved DNA sequences which play a role in regulating the immune response.

Dr. Hood has now sequenced over 90,000 base pairs from mouse DNA and 50,000 base pairs from the human T-cell receptor locus. Through these studies he has not only made advances in DNA sequencing technology, but new biological insights have emerged as well. He has gained insight into gene segments involved in generating T-cell receptor diversity and has also revealed a 120 base pair segment in a non-coding region that is similar in a diverse set of organisms. Preliminary studies suggest that it may have an important regulatory function. As the large-scale sequencing projects complete the initial phase, those that are successful will be ready to expand into a more production-oriented phase in FY 1993.

Model Organisms

Studies of the genomes of model organisms will help us understand more about the human genome. For example, approximately 90 percent of the gene-rich region of the genome of the fruit fly has been cloned and mapped using the yeast artificial chromosome (YAC) cloning system. The clones are being assembled into contigs--overlapping, ordered segments; currently, the largest contig from the fly genome is four million base pairs in size. These clones have been made available to the large community of researchers studying the fruit fly. Published reports of the successful isolation of a number of genes are now emerging from this work. Much of this information will be useful in identifying, isolating, and understanding related human genes.

The genetic map of the genome of the mouse is approximately one-third complete. Over 1,000 genes and DNA markers have been mapped. To make the mouse genetic map more useful to researchers studying the human genome, scientists at the Jackson Laboratory in Bar Harbor, Maine are assembling data for comparative maps of the mouse and human genomes. Information about the location of a gene on the mouse map allows one to predict with 90 percent probability where the gene will map on the human chromosomes and vice versa. Today, approximately 700 loci have been mapped in both mouse and humans and 61 regions in which gene order is the same in human and mouse have been identified. Further work on the maps of the fruit fly and the mouse will continue to support the efforts to map the human genome.

Technology Development

Technology development in the areas of genome mapping, DNA sequencing, and informatics is a key component of NCHGR scientific efforts. During FY 1991, over $11 million was devoted to this objective. In addition to traditional grant mechanisms such as regular research projects and Small Business Innovative Research grants, the NCHGR has utilized exploratory and developmental grants to stimulate research and provide support for high-risk, high-payoff projects, particularly projects bringing together teams of interdisciplinary researchers. In addition to these individual investigator grants, each of the NCHGR supported human genome research centers has a significant technology development component.

Databases and Biological Resources

One of the purposes of the Human Genome Project is to develop and provide improved research tools and resources to the biomedical research community to facilitate research in human and molecular genetics. Scientists working in genomics, genetics, molecular biology, and cell biology need cloned genes and DNA segments that have been mapped, as well as information about those genes in the form of electronic databases. As the genome project progresses, the need for and complexity of such resources will increase as the amount of information increases.

In order to gain the maximum benefit from the genome mapping and sequencing data being developed in laboratories worldwide, mechanisms must be in place for rapidly distributing research results. The quantity and complexity of the data demand flexible, computer-based systems that are capable of handling not only the anticipated individual data items, but also provide researchers with tools for creating new linkages and correlations among the diverse data elements. The NCHGR is committed to the development and support of such resources.

Genome Data Base

The Genome Data Base at Johns Hopkins University collects, edits, and distributes human genetic mapping data and maps of several types in support of genome research. It currently supports more than 3,000 registered users worldwide. Originally developed with support by the Howard Hughes Medical Institute, the NCHGR and the Department of Energy human genome program undertook joint funding in FY 1991. Project review and management are currently performed cooperatively by the two agencies, which plan to make this database a truly international effort.

Databases for Model Organisms

To facilitate genomic research in selected model organisms, NCHGR has solicited applications to develop and operate databases of genetic and physical mapping data for yeast, Drosophila, and mouse.

Recognizing the need for rapid communication of their research data, experts in yeast, Drosophila, and mouse genome mapping have formed collaborations with computer scientists and database experts and are in the process of designing databases to serve their respective communities. By FY 1993 these projects will be well underway and will require significant funding.

Sharing Databases Between Human Genome Research Centers

NCHGR has encouraged collaboration among the data management staffs of the NCHGR and Department of Energy-funded human genome research centers. These collaborations are now beginning to bear fruit in the form of joint research and development efforts directed toward laboratory data management systems and public databases for rapid sharing of the centers' research results. The first such database to come online is expected to be one that contains the results from a joint Baylor University - University of Michigan project to screen a chromosome 17-specific YAC library (see below). In addition to the computational staffs from Baylor and Michigan, this project is benefitting from collaborations with members of the MIT and University of Utah human genome research centers.

Joint YAC Screening Effort

NCHGR has established two YAC screening programs to facilitate access by the broad community to the fruits of genome research. These programs serve researchers working on chromosomes 17 and 21. Developing and working with YAC libraries--complete collections of human DNA cloned in YAC vectors--is still labor intensive and difficult and is beyond the reach of many small laboratories. Therefore, Dr. David Patterson of the Eleanor Roosevelt Institute for Cancer Research in Denver, Colorado is offering screening of YAC libraries for genes or DNA sequences of interest to any investigator and providing the identified YAC clones to the investigator. The identity of the clones will be made known to all participants in the Joint Screening Effort.

A similar broad collaboration for the identification of YACs derived from human chromosome 17 has been established by Dr. David Ledbetter at the Baylor College of Medicine in Houston, Texas in collaboration with Dr. Francis Collins at the University of Michigan in Ann Arbor.

Mapping Genes on Chromosomes

Many investigators have genes or DNA fragments that they wish to localize on human chromosomes but do not have the resources or technology available in their own laboratory. To assist them, the NCHGR supports two major laboratories that provide gene mapping services. Dr. Uta Francke from Stanford University and Dr. Thomas Shows of Roswell Park Cancer Institute, have been particularly active in mapping genes to chromosomes to support not only their research, but the research of many other "gene hunters." These scientists are making a significant contribution to this effort. Approximately 1,700 functional genes have been mapped and these two researchers have mapped, over the years, more than 20 percent of the genes that have been localized to human chromosomes.

Cell Lines Available to Community

In FY 1991, NCHGR continued to provide support for the transfer of a set of more than 600 cell lines widely used for genetic mapping studies to the Human Genetic Mutant Cell Repository in Camden, New Jersey. Prior to the acquisition of these cell lines by the Cell Repository, only those scientists collaborating with the Centre d'Etude du Polymorphisme Humain, an organization located in Paris, France, were able to obtain the DNA from these cell lines. Now the cell lines are available to all interested scientists in the research community.

Ethical, Legal and Social Implications

Clinical Integration of New Genetic Tests

The scientific advances generated by the Human Genome Project will speed up the process by which genetic testing capabilities become available for clinical use. It is therefore imperative that mechanisms for the delivery of genetic services are examined and refined. As new markers are identified, questions will arise such as for whom is such testing most useful? Should children be tested? How will the implications of test results for extended family members be disclosed and the confidentiality of the information protected from third parties? To address such questions, the NCHGR has initiated a 3-year research program involving several NIH components to define the best methods for educating and counseling individuals who want to be tested for cystic fibrosis mutations. Seven research teams across the country will conduct eight studies to assess interest in CF testing among different populations, identify methods for increasing a person's understanding of the implications of carrier status, and develop ways to protect individuals and families from psychological harm, stigmatization, and discrimination based on their test results. The practices that are established for the use of the genetic test for cystic fibrosis will be relevant to many genetic tests developed in the future. For example, NCHGR has already been working with the National Cancer Institute to develop a joint research initiative to explore the best way to utilize genetic tests for susceptibility to various cancers such as breast and colon cancer. Such tests are expected to be available in the near future. A joint initiative will be developed in FY 1992 for funding in FY 1993.

Genetic testing and insurance

The private insurance industry is still in the process of establishing its own policies with respect to genetic testing and genetic information. As more people become aware of their genetic risks, commercial insurers will have to decide whether to include such information in their underwriting decisions. The Health Insurance Association of America and the American Council of Life Insurance have agreed to work with the NIH-DOE ELSI Working Group in developing their policy. A multi-disciplinary task force of grantees, consultants, consumers and insurance industry officials, has been established to examine the issues commercial insurers and their clients face and to develop recommendations for professional and corporate policy. The task force plans to issue a preliminary research report in 1992, and a final report outlining policy options in May 1993.

Privacy of genetic information

As more genetic factors in disease are identified, increasing amounts of genetic information about individuals will be gathered and stored in sites removed from the regulated setting of the biomedical research laboratory. In addition to genetic registries compiled by health voluntary organizations for research purposes, genetic information will increasingly appear in family physicians' medical records, the records of health care insurers and employer-based health benefits plans. Guidelines need to be developed to provide uniform protections across these many different private sector settings. Through its ethics working group, NCHGR is working with voluntary health organizations, health professional organizations and privacy experts to develop proposals for such guidelines. These proposals will be promulgated during FY 1993. The NCHGR will sponsor discussions to disseminate its proposals regarding research and private sector uses of genetic data, and encourage consensus development on the issues among relevant policy makers.

Educational Activities

Ultimately, the best way to decrease the risk of genetic discrimination and increase the beneficial uses of new genetic knowledge is to promote better understanding of human genetics and to involve the public in deliberations over its use. NCHGR is stimulating an active program of public discussion and education, through a series of educational training projects and public fora. The educational projects initiated to date include high school teacher training programs at two major genome research centers, short courses for college biology faculty, and a series of workshops on genome research and its social implications targeted to state government officials, primary care health professionals, and science journalists. In addition, over 18 meetings devoted to public discussions of the social implications of genome research have been held, with NCHGR support, in 13 states and the District of Columbia. These meetings are complemented by NCHGR support for a 10-part public television series now in production entitled "The Future of Medicine," which will explore the public impact of genome research. This series will provide more focus in FY 1993 for local and regional public educational activities coordinated by the NCHGR. It will be complemented by a national, interactive tele-course on genetics and society designed for high school level science and social studies classes.

Minority Activities

The NCHGR has supported several projects to recruit minority scientists and students who wish to pursue a career in genomic research into the Human Genome Project. Through the Minority Institution Travel Award Program, the NCHGR supports travel to meetings or to attend specialized courses. For example, two faculty members from Clark-Atlanta University and the University of Puerto Rico attended a 3-week course on mammalian genetics and a faculty member from Howard University was supported to attend a major international conference on human gene mapping.

Through the National Research Service program, NCHGR supports minority predoctoral students who are pursuing training in scientific disciplines relevant to genomic research. Currently, students are studying at a number of major universities under NCHGR support, including Harvard University, University of Pennsylvania, University of Texas, Albert Einstein College of Medicine, and the Massachusetts Institute of Technology.

NCHGR is also supporting faculty who wish to pursue research projects relevant to the Human Genome Project. For example, a planning grant was recently awarded to investigators at Howard University College of Medicine who wish to establish cell collections from African-American families for genetic studies. This resource will augment existing collections which contain samples mostly from Caucasians. NCHGR is committed to continuing and expanding these activities in future fiscal years and hopes that some of the pilot projects will succeed in developing into full-scale grants.

National Center for Human Genome Research

Research Management and Support

Authorizing Legislation - Section 301 and 487 of the Public Health Service Act. 1992 Authorization: Indefinite

Budget Authority:

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
37	$3,717,000	45	$5,488,000	51	$5,757,000	+6	+$193,000

This activity provides the staff and resources that support the overall administrative and scientific management of the National Center for Human Genome Research.

Organizationally, the NCHGR is composed of the Office of the Director, the Office of Administrative Management, and the Office of Genome Communications and the following components which manage the Center's extramural program activities: the Office of Scientific Review, the Research Grants Branch, and the Research Centers Branch.

The Office of the Director provides overall policy and program direction and professional leadership to the NCHGR. The Office of Administrative Management provides financial management, administrative and human resource management, planning and evaluation, legislative liaison, administrative grants management, and staff support to the Program Advisory Committee on the Human Genome and the National Advisory Council for Human Genome Research. The Office of Communications manages a broad communications program aimed at disseminating information about the NCHGR and the Human Genome Project.

The extramural review staff provide policy direction and coordination for all phases of scientific and technical review of research grant applications, while program staff provide the planning, development, scientific administration and monitoring of human genome research grants, research centers, research training and fellowship programs.

Funding for the research management and support activity follows:

Year	Amount	FTE
FY 1990	$2,811,000	26
FY 1991	3,717,000	37
FY 1992	5,488,000	45

Rationale for the Budget Request

The FY 1993 request for the research management and support activity is $5,757,000, an increase of 4.9 percent over the FY 1992 estimate. This increase will provide for pay-related and other inflationary increases.

NATIONAL INSTITUTES OF HEALTH

National Center for Human Genome Research

Detail of Permanent Positions

	1991 Actual	1992 Appropriation	1993 Estimate
ES-4..............	1	1	1
Subtotal.......	1	1	1
GS/GM-15...........	7	7	7
GS/GM-14...........	4	4	5
GS/GM-13...........	4	7	8
GS-12..............	3	4	5
GS-11..............	2	2	2
GS-09..............	2	3	3
GS-08..............	1	1	1
GS-07..............	12	14	15
GS-06..............	1	1	1
GS-05..............	4	4	5
GS-02..............	--	1	1
Subtotal......	40	48	53
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Full Grade.........	--	1	1
Subtotal.........	--	1	1
Unfilled positions, end-of-year......	4	--	--
Total permanent positions......	45	50	55

NATIONAL INSTITUTES OF HEALTH

National Center For Human Genome Research

New Positions Requested

Research Management & Support	Grade	1993 Number	 Annual Salary
Health Science Administrator (ELSI).	GS-14	1	$ 56,427
Health Science Administrator........	GS-13	1	47,750
Program Analyst....................	GS-12	1	40,156
Writer/Editor......................	GS- 7	1	22,636
Grants Technical Assistant..........	GS- 5	1	18,276
		5	185,245

NATIONAL INSTITUTES OF HEALTH

National Center for Human Genome Research

AMOUNTS BUDGETED FOR INCREASES IN
FULL-TIME EQUIVALENTS

ACTIVITY/POSITIONS	GRADE	NO. OF POS.	O.C.11 ANNUAL SALARY	O.C. 12 BENEFITS 18.9%	O.C. 21 TRAVEL	O.C. 23.1, 23.2 RENT	O.C. 23.3 COMM/ UTIL	O.C. 25 OTHER SERVICE	O.C. 31 EQUIPT.	OTHER OBJECTS	SUB.TOT. NEW COSTS	SUPPORT STAFF SHARE	NO. OF FTE	TOTAL NEW COSTS
NCHGR Res. Mgmt. & Support														
Health Science Administrator	GS-14	1	$56,427	$10,665	$4,000						$71,092	$7,244	1.0	$78,336
Health Science Administrator	GS-13	1	47,750	9,025	4,000						60,775	7,244	1.0	68,019
Program Analyst	GS-12	1	40,156	7,589							47,745	7,242	1.0	54,987
Writer/Editor	GS- 7	1	22,636	4,278							26,914		1.0	26,914
Grants Technical Assistant	GS- 5	1	18,276	3,454							21,730		1.0	(21,730)
Secretary	GS- 5	1	18,276	3,454							21,730		0.8	17,384
		6	203,521	38,465	8,000	0	0	0	0	0	249,986	21,730	6	$245,640

The NCHGR has a 15-year time clock for attaining our stated goal. Management of the Human Genome Project requires considerable amounts of data collections, analysis, and integration as well as the organization of numerous meetings and workshops. The appropriate monitoring of grantees and grantee results will allow NCHGR to evaluate progress and steer the Human Genome Project in the right direction. The scientific vacancies, once filled, will assist in evaluating and monitoring in the areas of Model Organisms and the Ethical, Legal and Social Implications of genetics research. An additional program analyst is needed to monitor and evaluate progress towards attaining the 5-year goals of the Human Genome Project. The Office of Communications is responsible for responding to the media, other countries, and the scientific community about the goals and progress of the NIH Human Genome Project. Appropriate clerical support is needed for these new individuals and those currently on-board.

NATIONAL INSTITUTES OF HEALTH

National Center for Human Genome Research

Advisory and Assistance Services

In FY 1993 the NCHGR's consultant services requirements total $281,000, an increase of $9,000 over the FY 1992 estimate. The NCHGR utilizes consultant services to support the Program Advisory Committee on the Human Genome, which provides guidance on program direction, and the National Advisory Council for Human Genome Research, which provides scientific and technical expertise to the Center that are essential to the peer review process. The increase from FY 1992 to FY 1993 reflects a modest increase for inflation.

The NCHGR continues to play a major role in sponsoring and hosting meetings, bringing together investigators with common research objectives and encouraging collaboration, the exchange of materials and the use of compatible protocols where appropriate. In addition, meetings are held to bring together professionals from several different disciplines, such as law, ethics, and industry to address key issues, develop recommendations, and suggest strategies for dealing with the social, legal, and ethical sequelae of human genome research.

The personnel appointment mechanism is used to support the Program Advisory Committee on the Human Genome and the National Advisory Council for Human Genome Research. These advisory groups each meet three times yearly to provide overall guidance to the NIH. The groups have representatives from industry and academia and represent the broad range of scientific expertise needed to oversee the Human Genome Project.

Policy guidelines exist in the from of OMB Circular A-120, Guidelines for the Use of Advisory and Assistance Services, and DHHS General Administrative Manual 8-15, Advisory and Assistant Services. This guidance has been promulgated to make staff aware of the definition of Advisory and Assistance Services (AAS). The NIH Accounting System contains Common Accounting Numbers (CAN's) that have been designated for use in identifying and aggregating costs for AAS. Additionally the center has established a review process involving all appropriate administrative and management personnel. Proposals are reviewed by the Administrative Officer, the Committee Management Officer, the Budget Officer, the Executive Officer, appropriate branch managers, and the Deputy Director, as necessary.

WEDNESDAY, MARCH 25, 1992.

NATIONAL LIBRARY OF MEDICINE

WITNESSES

DR. DONALD A.B. LINDBERG, DIRECTOR, NATIONAL LIBRARY OF MEDICINE

DR. BERNADINE P. HEALY, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

KENT A. SMITH, DEPUTY DIRECTOR, NATIONAL LIBRARY OF MEDICINE

DR. HAROLD M. SCHOOLMAN, DEPUTY DIRECTOR FOR RESEARCH AND EDUCATION, NATIONAL LIBRARY OF MEDICINE

KENNETH G. CARNEY, EXECUTIVE OFFICER, NATIONAL LIBRARY OF MEDICINE

SUSAN U. LEVINE, BUDGET OFFICER, NATIONAL LIBRARY OF MEDICINE

DENNIS P. WILLIAMS, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN

INTRODUCTION OF WITNESSES

Mr. NATCHER. At this time we take up the budget request for fiscal year 1993 for the National Library of Medicine.

We have before the Committee, Dr. Donald A.B. Lindberg, Director.

Dr. Lindberg, it is a pleasure to have you before the Committee. Before you give us your statement tell us who you have at the table with you.

Dr. LINDBERG. Thank you, Mr. Chairman.

On my right is Kent Smith, Deputy Director; Sue Levine, Budget Officer; and Ken Carney, Executive Officer, is to her left.

Mr. NATCHER. We will be pleased to hear from you.

OPENING STATEMENT

Dr. LINDBERG. It is a pleasure to be here before you once again. We are proud of the National Library of Medicine and its performance during the last year. There have been many changes.

It is ironic that with the collapse of the Soviet Empire we are now finally able to complete an agreement with the Russian National Library of Medicine that has been pending for 20 years.

The Eastern Europeans are interested as well in joining our system and getting access to biomedical literature. We will have an opportunity to sponsor a meeting in Geneva in September of Eastern Europeans.

There is an Office of Health Services Research Information that has been created at the National Library of Medicine in collaboration with the Agency for Health Care Policy and Research.

The Agency releases clinical guidelines that are now part of the on-line system.

The Library's National Center for Biotechnology Information, now two years old has a responsibility to deal with molecular biology information and mapping data that derive from the human genome project. The Center participated in a milestone accomplishment I would like to describe to you.

In October 1991, we issued a press release announcing the discovery of the gene for a genetic illness called Kallmann's syndrome. Scientists at the Institute Pasteur in Paris had narrowed the possible location to 600 sequences. Somewhere in there was the gene, the question was, where? Using the new computer communication networks, the French scientists sent the data to Bethesda, to a scientist named Jean Claude Claverie. He used computer programs developed at the National Center for Biotechology Information to find the gene for Kallmann's. He discovered that it was similar to genes that produce a protein that regulates nerve growth in the embryo, and by a quick process of deduction was able in quick collaboration with colleagues at Pasteur to confirm its function.

This is one example of the fruits of molecular genetics and of the genome that lie ahead.

Another accomplishment this year was the release of a second CD–ROM for the Unified Medical Language System and its Metathesaurus. This project was supported by the Committee with special earmarked funds and has been a great success. The goal is to make it easier to map scientific knowledge to the problems faced by scientists and clinicians. This UMLS work is a critical part and important contribution to the Administration's stated initiative on high performance computing and communications. There is also progress on our Grateful Med software which is a user-friendly system that lets doctors search our data base.

Today this is the predominant method of Medline access. Eighty percent of our U.S. users use that system.

I would like to tell you a brief story that has to do with Grateful Med. There were 6,000,000 on-line searches. I am choosing just one.

This story was sent to me by a California physician. He was presented with a problem of a man who was being evaluated for a heart transplant. That is fairly dramatic. The doctor, working at home on his personal computer, thought he could find a way around that problem.

He used the Grateful Med software to connect to Medline and gather abstracts about the problem. He came to the conclusion that the symptoms had to do with the drug being used on the patient and he found a different therapy. So, sitting at home in California and using a data base in Washington, the doctor found an article in a Belgian journal that eliminated the need for a costly and risky heart transplant.

It is that sort of thing that makes me very determined that all American health care practitioners have access to the products and services of the National Library of Medicine. They all ought to share in those benefits.

It is easy to imagine someone in a remote part of the country requiring specialized knowledge to treat a patient. That need is what our outreach program is addressing. We are making special efforts to reach practitioners serving minority populations and rural areas. I can point with some pride to the accomplishments of the Library in terms of outreach.

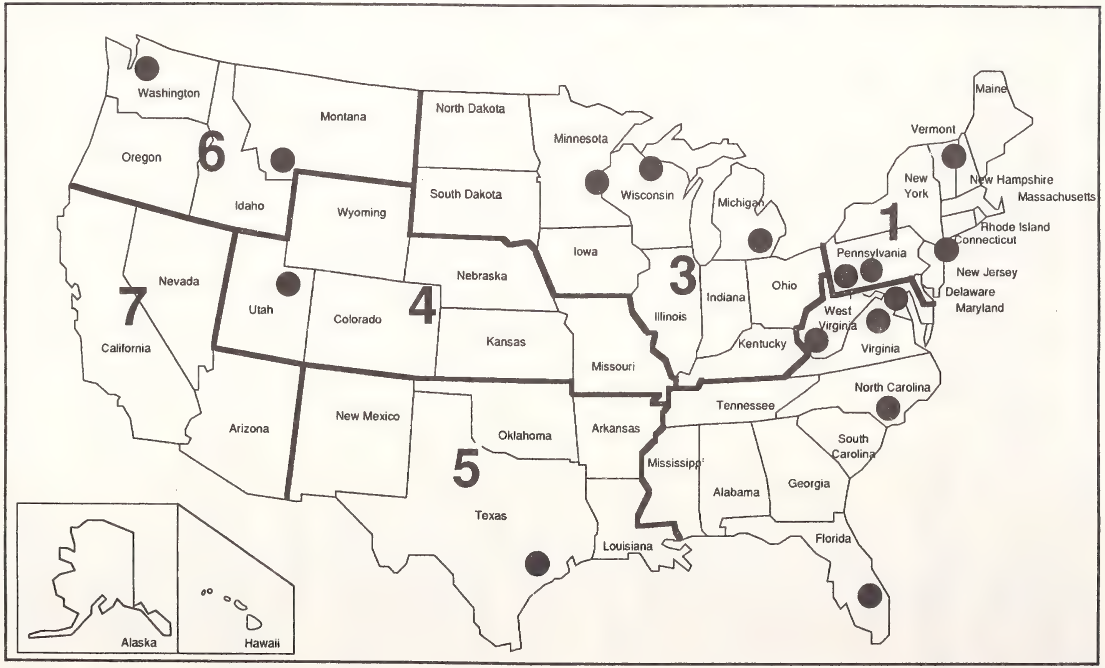
We have distributed to you, maps that illustrate how, with money earmarked for outreach first given to the Library in 1990, we have really done a good job, although perhaps not as much as Dr. DeBakey and the outreach committee had in mind.

[The information follows:]

MAP 1

National Library of Medicine Outreach

September 30, 1989



National Network of Libraries of Medicine

7 RML's
125 Resource Libraries
3500 Member Institutions

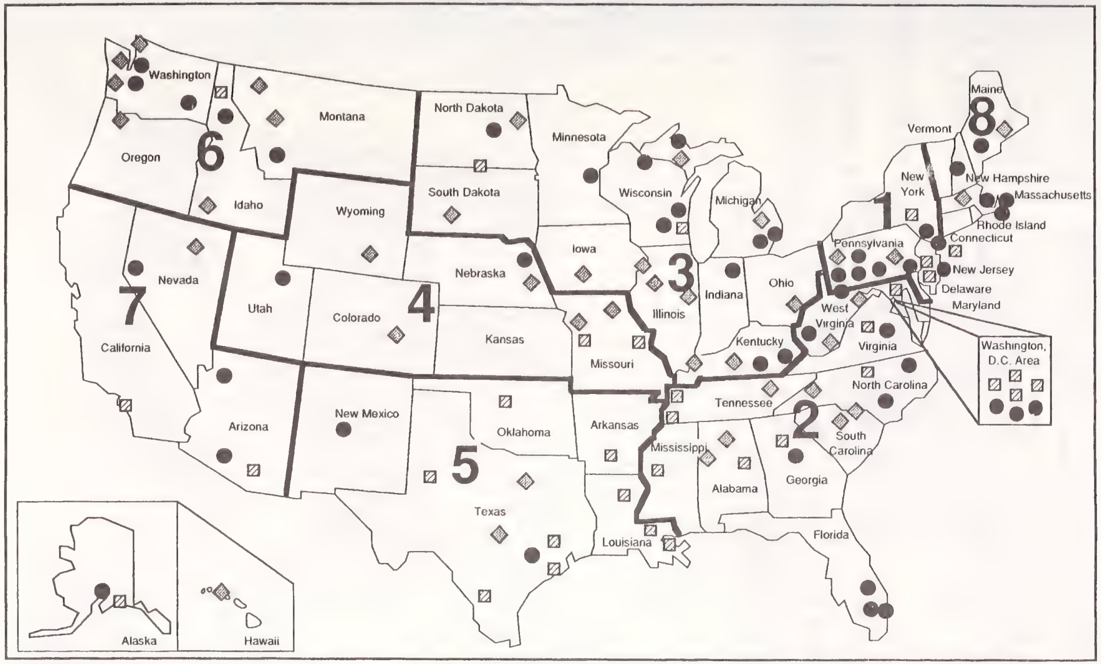
● Grants to Improve Local Information Services (16)

Total: 16 Projects

MAP 2

National Library of Medicine Outreach

September 30, 1991



National Network of Libraries of Medicine

8 RML's
135 Resource Libraries
3600 Member Institutions

● Grants to Improve Local Information Services (48)

◈ Introducing GM to Rural Health Professionals (39)

▨ Outreach to Minorities (33)

Total: 120 Projects

Map 1 shows that before the money we did award grants to improve local services. Two years later in 1991, we have very much more in the way of activity. As you can see, on map 2, we now have many projects throughout the country that are aimed specifically at health professionals serving rural areas and minority populations. Often these projects are overlapping and serving multiple purposes.

How do we measure the efficacy? One way is by measuring growth in access to our own information systems.

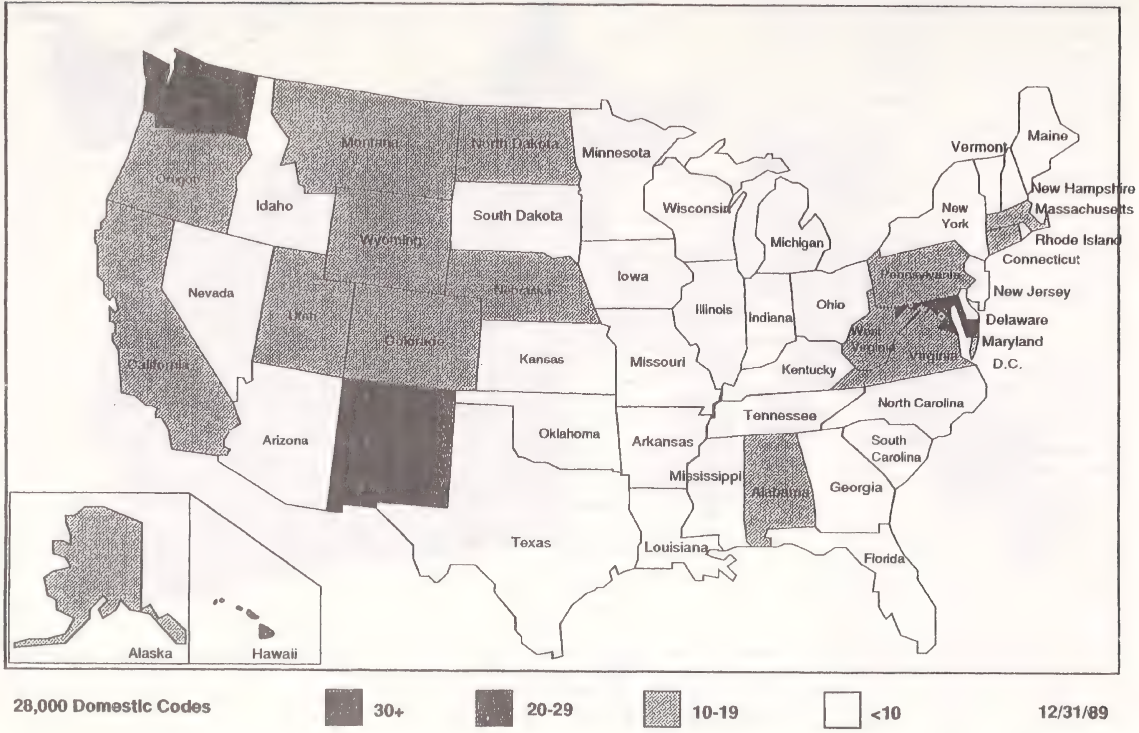
In maps 3 and 4, we are showing the number of persons who are able, by virtue of having gotten access codes, to call up and use our online system when they need it. Like that doctor in California.

[The information follows:]

MAP 3

National Library of Medicine Access Codes per 100,000 Population

1989

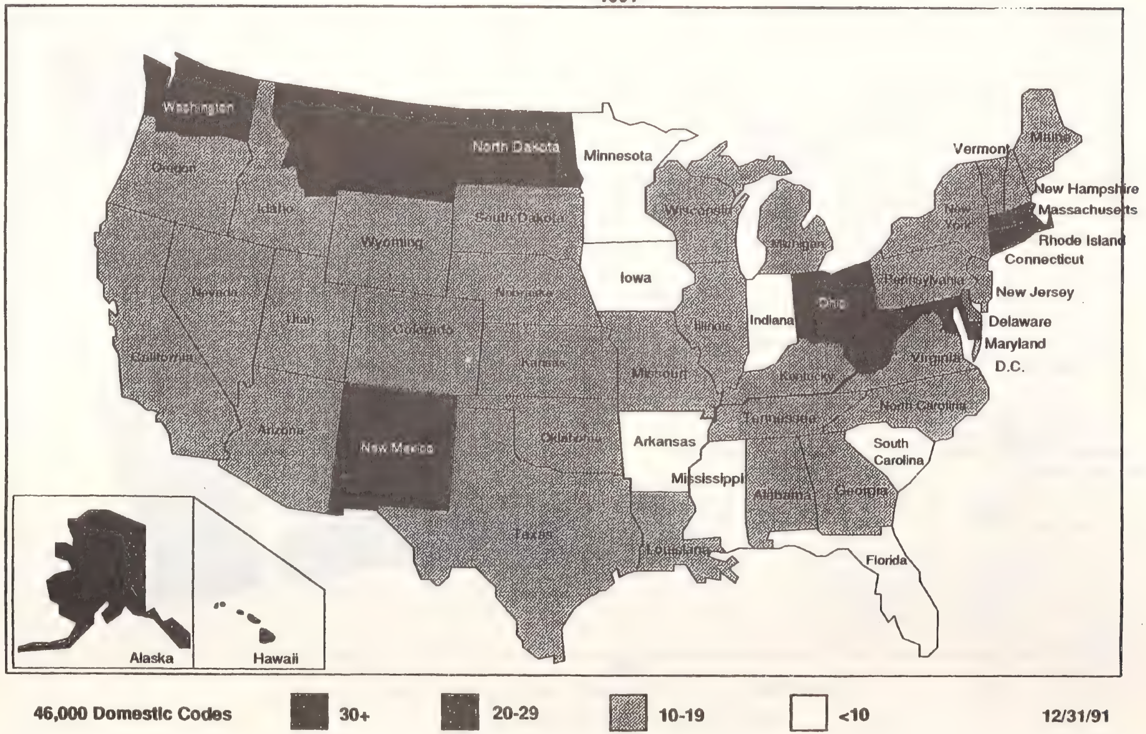


28,000 Domestic Codes

12/31/89

MAP 4

National Library of Medicine
Access Codes per 100,000 Population
1991



My goal is that all American health care practitioners have access codes to be able to use the system when they need it.

In the first illustration—map 3—we see that much of the country does not have too much in the way of those codes. When we turn to map 4, we see great improvements in the spread of user codes.

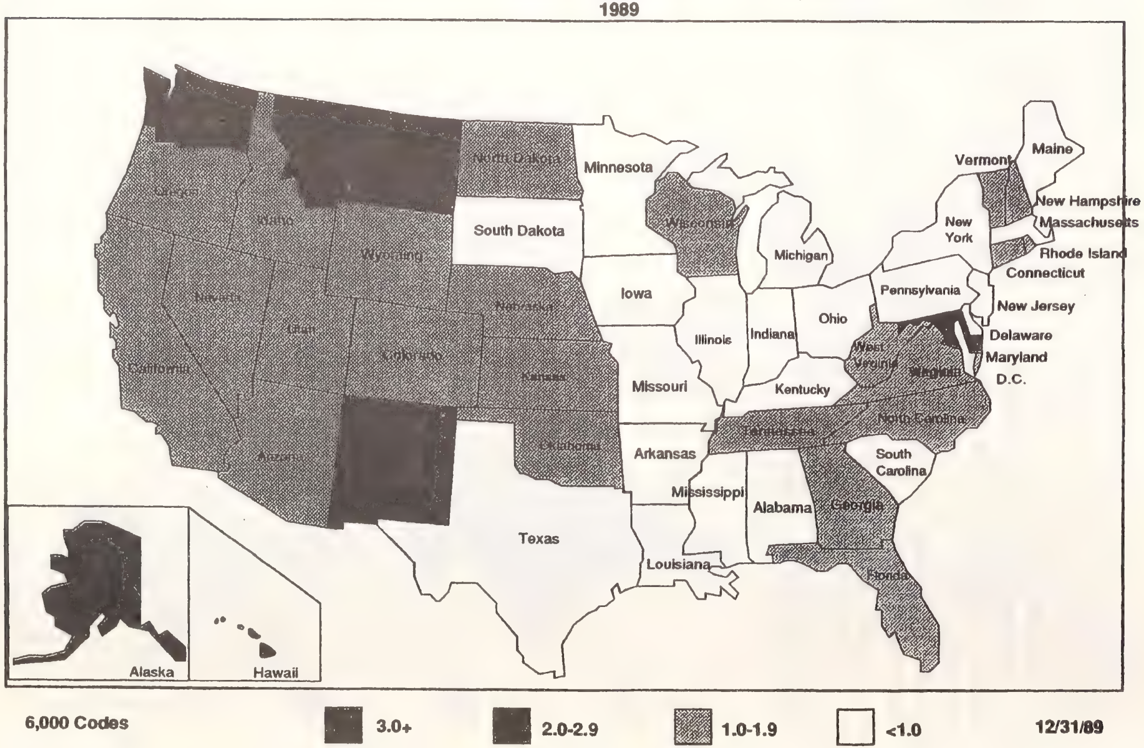
Although there is encouraging headway, there are still areas like Mississippi, South Carolina, Florida, Iowa, Indiana, and Minnesota that are not yet up to par.

These last two slides show the same data but they are normalized against the populations. I don't think they changed the patterns too much. It suggests we are doing better in the West than we thought but there is still a long way to go.

[The information follows:]

MAP 5

National Library of Medicine
Physicians' Access Codes per 100 Physicians
1989

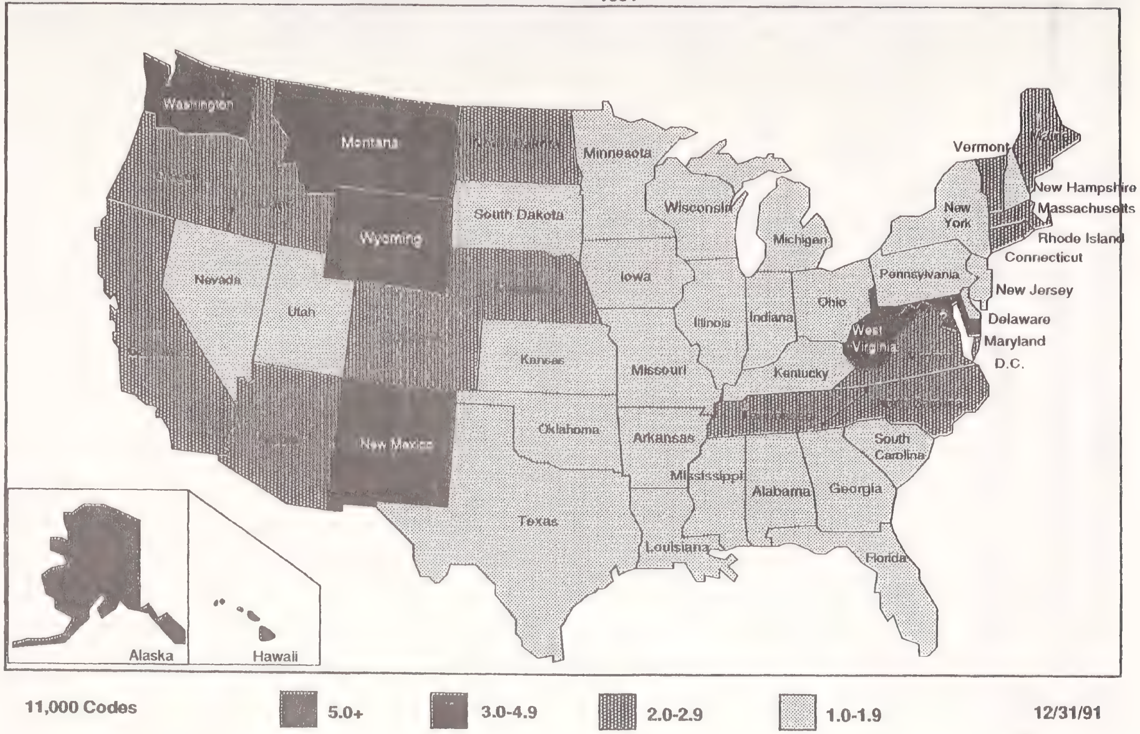


6,000 Codes

12/31/89

MAP 6

National Library of Medicine
Physicians' Access Codes per 100 Physicians
1991



11,000 Codes

12/31/91

Mr. Chairman, I appreciate your patience in listening to this report.

I am most grateful to the Committee for your support in the past.

[The statement of Dr. Lindberg follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement of the Director
National Library of Medicine

Mr. Chairman and members of the Committee: I wish to begin my statement by recounting two events involving the National Library of Medicine in 1991. The first is an incident of the sort we hear more and more of from users of the Library's services.

A California endocrinologist, at home on a weekend, received a call from a colleague. A patient at the hospital was presenting with Amiodarone toxicity and hyperthyroidism, uncontrolled; he was not responding to usual treatment. If prolonged and persistent, this condition produces cardiac toxicity and can result in death. Because of his unresponsiveness, the patient was being considered for a heart transplant to be done at the Stanford University Medical Center.

From his home, the endocrinologist did a rapid search of the National Library of Medicine's journal literature database, MEDLINE. Using a personal computer program developed by the NLM, called Grateful Med. He discovered an article in a Belgian journal that suggested a new treatment, verified this approach with another search, began the suggested treatment, and the patient responded rapidly and was able to be discharged in five days.

I believe that this incident illustrates perfectly the potential benefits of online literature searching using Grateful Med:

Convenience--searching may be done at home, office, or hospital.

Simplicity--it requires typing only a few words on a microcomputer.

Speed--from turning on the PC to reading the abstracts--about 5 minutes.

Effectiveness--finds a few pertinent articles among MEDLINE's millions.

Economy--the cost of finding the articles was less than $3.

The second event was a discovery of the sort one would expect to hear announced by an NIH laboratory or a university, rather than a library. In October 1991, the NLM announced the discovery of the gene responsible for Kallmann Syndrome, a rare genetic disease characterized by the bizarre association of infertility and a lack of the sense of smell. The discovery, by an international team from the Library's National Center for Biotechnology Information and the Pasteur Institute in Paris, depended as much on high-speed computer networks and genetic sequence databases as on traditional laboratory methods. A large chunk of DNA information was sent by electronic mail to the Library, where the important parts of the Kallmann gene were identified using computer tools developed at NLM. The discovery represents an important advance in scientists' understanding of nerve-cell migration and brain development that may ultimately result in the development of new drugs to promote accurate nerve regeneration in humans.

Recent Congressional initiatives for the Library have dealt with outreach to health professionals, high performance computer and communications, and the creation of a National Center for Biotechnology Information. It is through initiatives such as these that we are able to report the progress and breakthroughs I've just described.

NLM's outreach efforts have resulted in physicians, researchers, and health science educators enrolling in NLM's online network in record numbers. There are now more than 50,000 network members. These users did some 6 million searches on the Library's major database, MEDLINE, covering general medical literature, and our more specialized databases in AIDS, cancer, hazardous wastes, and other subjects of contemporary concern. This increasing demand by health workers for up-to-date information has, in turn, presented NLM with the welcome challenge of providing the necessary basic library services that are essential to undergirding these new national initiatives. I have some charts that I will submit for the Committee record that graphically show the success of the outreach initiative and the increasing demand for library and information services.

The composition of the NLM's online network has shifted radically over the last five years since the introduction of the microcomputer software, Grateful Med. Where once our users were made up almost exclusively of skillful health science librarians and information specialists, today the great majority of those joining the network are individual users in the health field--health professionals and students. This shift is the result both of new technology and of the nation's medical librarians diligently training health professionals to use these new tools.

Two important new network capabilities were introduced in 1991. The "clinical alert" service has proven to be a valuable method of making important research information instantly available on the Library's online network. Clinical alerts accelerate the speed with which potentially life-saving medical information from NIH is disseminated to the practicing community. Seven alerts were made available to online users last year and also sent separately to medical libraries in the national network for rapid distribution within their institutions.

The second major enhancement to the network in 1991 was the introduction, in May, of "Loansome Doc." Loansome Doc allows Grateful Med users to place an online order for a copy of the full article for any reference material retrieved from MEDLINE. Such articles can be immediately faxed to the physician's office if so desired. This capability is facilitated by health sciences libraries in hospitals and other institutions around the country that agree to serve the Grateful Med users. Although this service is less than a year old, a number of health professionals have taken the time to detail their experience with Loansome Doc. For example, one of the staff at the regional hospital in Bethel, Alaska, said that a MEDLINE search was immediately conducted for a patient seen at 11:00 a.m., by 2:00 p.m., the staff had received via Loansome Doc the two articles they needed to guide their treatment. The articles were faxed from the hospital library in Anchorage, some 400 miles away.

On the theory that NLM's information services are not fulfilling their potential if they are not serving the maximum number of health professionals, the Library continues to conduct a vigorous outreach program. It is unfortunately true that many American health professionals do not have easy access to computerized biomedical information--because of geographic isolation, non-affiliation with a hospital or medical school library, or simply because they lack information about the services available to them.

The outreach program intended to remedy this situation has been greatly aided by the member institutions of the National Network of Libraries of Medicine. New five-year contracts were signed in 1991 with the eight Regional Medical Libraries that, together with 130 Resource Libraries (primarily at medical schools) and 3500 local Libraries (primarily at hospitals), make up the Network. The new contracts emphasize Grateful Med training, demonstrations, exhibits, and other activities related to outreach.

NLM has used its authority under the Medical Library Assistance Act to further its outreach aims. Health science librarians and information specialists around the country have applied to NLM for support to help get the word out to their clientele. At hospitals, universities, and schools of the health professions, medical librarians are holding Grateful Med workshops and training sessions and they serve as a source of advice and consultation for the medical staffs and students. Their outreach has been especially valuable in small communities and rural areas, where the need is greatest.

The NLM has targeted some 30 grants and contracts to reach health professionals who serve minority populations. Prominent among these is a collaboration with Meharry Medical College in Nashville, Tennessee to develop an outreach demonstration project for health care practitioners including family practice residents who are in remote and professionally isolated settings. Another outreach effort, begun this year, will use the historically black colleges and universities to train medical and other health professionals in the use of NLM's toxicological, environmental, and occupational information resources.

A Long Range Planning Panel on Toxicology and the Environment was created in 1991 to review the NLM's toxicology-related information services and advise on their future direction. NLM is looking ahead, further into the 1990's and beyond, and assessing new information approaches to help in keeping man and the environment safe and healthy.

COMMUNICATIONS RESEARCH

The Library has two major components responsible for communications research and development: The Lister Hill National Center for Biomedical Communications and the National Center for

Biotechnology Information. The Library's grant programs also have a role in research and development, through funding investigator-initiated research applications, research career training in medical informatics at major universities, and the continuing support of Integrated Academic Information Management Systems at major universities.

The Lister Hill Center research programs apply state-of-the-art computer and communications technologies to the management of biomedical knowledge. An example of this work that has generated widespread interest in the biomedical community is the "Visible Human Project." NLM awarded a contract in 1991 for the first phase of a project to create, in complete anatomical detail, three-dimensional representations of the male and female human body. The "Visible Human Project"--building a digital image library of volumetric data representing a complete normal adult human male and female--will include digital representations derived from cross sectional photographic images from cryosectioning, computerized tomography, and magnetic resonance imaging of cadavers. The project is viewed as a first step in developing image libraries and as a test platform for developing methods and standards in this field.

The National Center for Biotechnology Information, mentioned earlier in connection with its role in discovering the Kallmann gene, also introduced in 1991 a new retrieval tool called Entrez which allows a scientist to search several hundred megabytes of sequence and MEDLINE data using techniques that are fast and intuitive. Such tools, by speeding up the identification of DNA responsible for genetic impairments, may play an increasingly important role in molecular biology research.

THE FUTURE

Several projects now under way at the Library may have the potential for profound influence on the way medical information is communicated. First, the Unified Medical Language System (UMLS) continues to make steady progress. Its goal is to overcome the many language-based barriers that health professionals face in retrieving computerized information. Among these barriers are (1) the variety of ways the same concepts are expressed in different computerized systems and (2) the difficulty in knowing which of many existing databases have relevant information sought. The Library has distributed a second experimental edition of the machine-readable "knowledge sources" as part of the UMLS. We hope to see applications developed in the next few years that will greatly improve the ease and efficiency with which health professionals have access to computerized information.

Another exciting area of activity is the multiagency High Performance Computing and Communications initiative. NLM is a lead medical organization in this program, with special interests in molecular biology computing creation and transmission of electronic images, the linking of academic health centers via computer networks, the creation of "intelligent gateways" to retrieve information from multiple life sciences databases, expanded training in biomedical computer science, and by connecting the nation's medical centers and hospitals to the newly emerging National Research and Education Network.

The National Library of Medicine is a unique national treasure. I wish to thank the Congress and this committee for supporting the Library over the years and for providing encouragement as we attempt to develop new and improved systems.

Mr. Chairman, the FY 1993 request for the National Library of Medicine is $108,662,000. I shall be pleased to answer any questions you may have.

LINDBERG, DR. DONALD A. B.
Director, National Library of Medicine

September 21, 1933. New York, New York

Education: A.B., Biology, Amherst College, magna cum laude, 1954; M.D., College of Physicians and Surgeons; Columbia University, 1958; Sc.D., Amherst College, (hon. caus.) 1979; Sc.D., State University of New York (hon. caus.) 1987; LL.D., University of Missouri-Columbia, (hon. caus.) 1990.

Professional History: 1984-present, Director, National Library of Medicine; 1988-present, Adjunct Professor of Pathology, University of Maryland School of Medicine; 1971-1984, Director, Information Science Group, University of Missouri School of Medicine; 1969-1984, Professor of Pathology, University of Missouri School of Medicine; 1976-1980, Director, Health Services Research Center with Special Emphasis Health Care Technology Center, University of Missouri-Columbia; 1972-1973, Consultant for Health Sciences to Vice President for Academic Affairs; 1969-1971, Professor and Chairman, Department of Information Science, University of Missouri School of Library and Information Science; 1970-1971, Staff, Vice President for Academic Affairs, University of Missouri; 1967-1970, Director, Regional Medical Program Information Systems; 1968-1970, Staff, Executive Director for Health Affairs, University of Missouri; 1962-1970, Director, Medical Center Computer Program, University of Missouri; 1962-1970, Director Medical Center Computer Program, University of Missouri; 1967-1969, Director, Missouri Regional Automated Electrocardiography System; 1966-1969, Associate Professor of Pathology, University of Missouri School of Medicine; 1963-1966, Assistant Professor of Pathology, University of Missouri School of Medicine; 1962-1963, Instructor in Pathology, University of Missouri School of Medicine; 1960-1963, Director, Diagnostic Microbiology Laboratory, University of Missouri Medical Center; 1960-1962, Resident Physician in Pathology, University of Missouri School of Medicine; 1959-1960, Assistant Resident in Pathology, Columbia-Presbyterian Medical Center; 1958-1960, Assistant in Pathology, Columbia University College of Physicians and Surgeons; 1958-1959, Intern in Pathology, Columbia-Presbyterian Medical Center; June 1955-Sept. 1955, June 1954-Sept. 1954, Research Assistant to Dr. O.E. Schotte, Amherst College.

Honors: Phi Beta Kappa; Simpson Fellow of Amherst College (1954-55); Markle Scholar in Academic Medicine (1964-69); Distinguished Practitioner in Medicine, National Academies of Practice in Medicine (1983); Member, Institute of Medicine, National Academy of Sciences (1985); Member of IOM Council (1990-93); Fellow, American College of Medical Informatics (1985); Surgeon General's Medallion, Public Health Service (1989); Nathan Davis Award for Outstanding Member of Executive Branch in Career Public Service, American Medical Association (1989); Walter C. Alvarez Memorial Award, American Medical Writers Association (1989); Presidential Executive Rank Award (1990); Fellow, American Institute of Medical and Biological Engineering (1992); Outstanding Service Medal, Uniformed Services University of the Health Sciences (1992).

Professional Memberships: Sigma Xi; American Society of Clinical Pathologists; College of American Pathologists (Telecommunication Network Committee, Committee on Emerging Technology); American Association for Advancement of Science; American College of Medical Informatics; Washington Society for the History of Medicine; Editor, Information Methods in Medicine, Lecture Notes in Medical Informatics, and Journal of Medical Systems; National Academy of Practice in Medicine Distinguished Practitioner; Computer Science and Engineering Board, National Academy of Sciences (1971-1974); U.S. Representative to International Medical Informatics Association and Trustee (1975-1984); Board on Health Sciences Policy, Institute of Medicine; President, American Medical Informatics Association (1988-1991); Board of Directors, International Medical Informatics Association (1992-).

Dr. Lindberg is the author of 4 books and more than 150 articles, reports, and chapters of monographs.

OUTREACH ACTIVITIES

Mr. NATCHER. Thank you, Dr. Lindberg.

Doctor, as you know, Dr. DeBakey's panel reported on Library outreach needs three years ago. With the pace of technology, do these recommendations need to be updated?

Dr. LINDBERG. Well, I think that the basic things that Dr. DeBakey and the panel pointed to were very, very accurate and those are the things we are trying to do. They naturally were enthusiastic in pointing out a number of things that NLM could do if they were funded at a higher level.

We proceeded basically in the priorities they established and they have been quite good.

Mr. NATCHER. Do you feel that the outreach activities in the past several years have met the main thrust as far as DeBakey's recommendations are concerned?

Dr. LINDBERG. I think they have. The Board of Regents added to those.

We got some personal help from Mr. Stokes in the area of outreach to minority populations. We knew we should do better but we didn't know quite how to do it. There are particular programs that I would call attention to in that area.

Training is one other problem for us. Dr. DeBakey and the other advisors were very anxious that we increase the number of medical people trained in computer work in biomedicine. We have had an opportunity to evaluate and renew the training grants competitively for another five years. So we have the basis for 10 new training grants. We are limited, in part, because of the failure of the reauthorization of the Medical Library Assistance Act.

DATA SYSTEMS

Mr. NATCHER. Last year you indicated that perhaps 15 to 20 percent of the country's health professionals use your data systems.

Has that improved since last year?

Dr. LINDBERG. We think it has probably improved another 5 to 7 percent partly because of our efforts to provide service directly and partly because of the companies that produce CD-ROM products that have Medline on them. We work in that respect hand and glove with the private sector. That has been a fantastic development.

People are delighted with these little ROMs and they can have the data locally on site. I should add that 60 percent of the sales of those are overseas.

I think that technology and our efforts have increased the usage of our information products, but we have a long way to go.

Mr. NATCHER. Can a doctor sitting at his office now obtain complete documents rather than summaries from your data systems?

Dr. LINDBERG. We are inching up on that problem, too, Mr. Natcher. As you know, some questions can be answered from the abstracts on the screen. When it is a serious matter like changing the treatment for a patient, you must read the paper, have the full information. In that case, it used to take some days to get information sent by mail. Today, however, it seems that faxes are everywhere. So, our systems have been changed. We have added to

Grateful Med a feature called Loansome Doc. It is l-o-a-n because we are doing an interlibrary loan.

It is a simple matter for the Grateful Med user, with one keystroke, to request that a copy of a full article come by courier or mail or by fax right away. When we added Loansome Doc, I thought it would be really wonderful to have the fax come in minutes, and it does, if you want it.

The librarians put another option in the program, and it was, "I will stop by the Library and pick it up on the way home." I told them that doctors did not do that. They drove straight to the golf course. The librarians insisted, and they were right, because 40 percent of the people choose the option to pick it up at the Library.

HIGH PERFORMANCE COMPUTING

Mr. NATCHER. Last year, you identified high performance computing as one of your top priorities. Do you still feel the same way?

Dr. LINDBERG. Yes. On the surface it would seem that high performance and outreach don't mix. It would seem that outreach is trying to expand today's services to benefit disadvantaged and rural populations and the high performance computing and communication systems (HPCC) are concerned with molecules and high science

But in reality, the way the Library does outreach is through communication networks. The communication network is a critical part of HPCC. I definitely would like to see NLM be a stronger player in the communications and computer aspects of biomedicine. The bigger field is largely in the hands of the Department of Defense, NASA, Energy, and NSF. But I think there is an important role for us, and we are happy to represent medicine then. For us, the two are top priorities and mutually supportive.

Mr. NATCHER. Will you describe to us your role in the Government-Wide High Performance Initiative? Will you be focusing on the development of the technology or its application?

Dr. LINDBERG. Largely the application, sir. There are four parts of it. I won't describe it all in great detail, but the first part is really the design and architecture of high performance computers. That is largely done by the Department of Defense. They don't need our help, and we have little to contribute in that side.

Where we have a great deal to contribute, and where the contribution has been welcome, is, as you said, in applications. We see our role in helping the biomedical center communities adapt to this new way of doing science, and even doing medicine. We want them to take advantage of these very high capacity transmission systems, as, for instance, with pictures.

There are lots of pictures—X-rays, CAT scans, PET scans, digital anatomy pictures—that allow you to create a scenario to do surgery, for example, or to make a synthetic hip device. It is easy to describe the uses, but it is hard to adopt that new technology, to get it in actual use in a hospital setting or a doctor's office. In addition, we use the high performance networks for assisting biomedical scientists in genome research. I think we will see before long the need to provide support for the ordinary clinics and the ordinary patient to utilize this new knowledge.

Mr. NATCHER. You have described your high performance computing activities as needing support for the institutions to connect with the high-speed network. Will medical schools have sufficient incentive to link into the system without Federal assistance?

Dr. LINDBERG. I think it will happen smoother and better if we can get in there with the grant program. NLM has had a grant program for 10 years called the Integrated Academic Information Management Systems, IAIMS. Originally, we encouraged the institutions to integrate all information services within the walls. Now we want to come back to those schools and say "the world is your oyster." You need to be connected to national and even international information sources. I think the schools that were advanced enough to start IAIMS planning 10 years ago are in the best position to take advantage of the new scheme, and those that are not must try harder. So, I would say that the country would benefit from an NLM effort to help them join those networks, yes.

USE OF PERMANENT PAPER

Mr. NATCHER. What recent progress have you made in persuading medical publishers to use permanent paper?

Dr. LINDBERG. I will pat the institution on the back, Mr. Natcher, but I have to start out by patting you on the back too. In 1987 we initiated a program at NLM to try to persuade publishers to pay attention to the bad aspects of acid-based paper, and the good aspects of alkaline paper, and the costs to society of not doing that. We had a meeting at which you gave the keynote address, and I must say that got their attention.

In those days, just 2 percent of the 3,000 journals that are published in Index Medicus had acid-free paper. Now, merely through meetings and presenting the information to them, and by finding a way to study the economics of publications, we have come to a point in just 5 years where 60 percent of the Index Medicus titles are on acid-free paper.

That was a good keynote address.

NATIONAL NETWORK OF LIBRARIES OF MEDICINE

Mr. NATCHER. I had a lot of help with that one. What can you tell us about changes in the regional library network in the last year.

Dr. LINDBERG. Yes, sir. There are two aspects of the changes. As you know, the idea of a National Network of Libraries of Medicine that a patient's doctor can get information anywhere in the U.S.—is taken for granted by young American doctors.

But in fact, the network did not exist before 1965. It was a direct result of the President's Commission on Heart Disease, Cancer and Stroke chaired by Michael DeBakey and Congress enactment of the Medical Library Assistance Act of 1965. It has evolved very nicely since then.

In the reorganization you referred to, we were able to accomplish two things: One was to increase the number of regional libraries from seven to eight. It is a recurring question: What is the best number? It started at 10, got to be 11, and then went down to seven. It was not quite adequate.

We put an additional library in the New England area. As it has happened in these renewal periods, there is competition for those libraries. That is probably a good thing, because even though I am not sure it doesn't cost the school something to be a regional library, they are very proud of doing it, and they do a good job.

Two things happened, because of an increase of funding in the outreach program earmarked by this committee. First, we were able to increase the number of regional libraries to eight, and, secondly, we could ask the people in those regional libraries to participate with us in our outreach initiative.

So, we essentially doubled the size of regional programs and in turn, these libraries were able to fund people to teach courses in how to search Medline using Grateful Med and other outreach related projects.

Mr. NATCHER. Mr. Stokes, I yield to you.

ACCESS CODES

Mr. STOKES. Dr. Lindberg, let me start with the maps there. On a couple of those pages, I see Ohio being blank. You need to explain that to me. It is page 3 and page 5.

Dr. HEALY. I noticed that, too, Mr. Stokes.

Mr. STOKES. You noticed that. You know, Worcester, Massachusetts, is taken care of. Can you explain those maps to me, where Ohio is blank?

Dr. LINDBERG. We would call your attention to the difference between three and four, because Ohio started out blank. That did not mean that it was completely void of worth and good medical talent, I am sure it had a lot. But by 1991, it had a considerable number of access codes, so we made considerable headway.

It has gone from the lowest to the highest level, actually.

Mr. STOKES. I notice Ohio has a little different color. What does that mean?

Dr. LINDBERG. That means Ohio has the highest participation.

MEDICAL LIBRARY ASSISTANCE ACT

Mr. STOKES. Dr. Lindberg, last year, in order to operate within fiscal limits, the Committee held the unauthorized programs at the fiscal year 1991 level. How did that affect the programs under the Medical Library Assistance Act?

Dr. LINDBERG. That was too bad for us. We understood the fiscal constraints on the Congress, but the net result for us was that the grants under the Medical Library Assistance Act lost $1,600,000 as compared with the President's 1992 budget, so it was unfortunate in that respect.

The categories that had to be cut out were the information access grants and also probably, most importantly, the training. The training grants were cut back severely. In fact, they are under by about $500,000. So that was too bad.

TRAINING GRANTS

Mr. STOKES. Have we kept up with the important initiative of training health professionals in the use of computer technology?

Dr. LINDBERG. No, I think we are not keeping up. I think we are doing an adequate job and not an outstanding job. That is what the DeBakey Committee said to us. The most common problem they found was the lack of skilled people. A school would create a post, and then have difficulty finding someone to fill it. They told us they wanted to increase the slots in the training grants.

Scientists are pretty determined about the importance of training in research in general and in this area in particular. We had to cut back 12 percent of the slots. We had 10 approved programs.

But we had to eliminate the slots, because of the cap funding. That is going in the wrong direction, from my point of view.

MINORITY ACCESS

Mr. STOKES. The Committee continues to be concerned about the poor health of the Nation's minority populations in both inner cities and rural areas. Tell us what the Library is doing to continue to provide access to its products and services to help provide access in these targeted areas.

Dr. LINDBERG. Well, some things in general: the first map that I showed, the 1992, not the 1991, points out some 120 projects. Some are large and some are small, but they are spread across the country. As the legend shows us, 29 are aimed at rural and 33 at minority populations, though sometimes they overlap.

In doing that, in no small part because of your advice, we are getting guidance as to how best to spend whatever money we can come up with. We started a program in Meharry which is doing very well, under which the school sends graduate students and medical students out into rural areas, and provides computer training for the students as they go out; doubling the benefit.

Again, partly because of the advice that you gave, we looked at our toxicology information programs, because we know minority populations are more at risk of toxicological problems at home and at work.

Dr. Melvin Spann of the NLM has initiated a program in which we make a special effort in nine selected Historically Black Colleges and Universities, to be sure that their faculty have training in NLM's automated toxicology systems. Also, I would like to introduce Dr. Charles Walker, who recently resigned as Chancellor of the University of Arkansas at Pine Bluff, and agreed to join us. He is a Professor of Pharmacology, so that is the closest to his heart, I guess. He has me sensitized about pharmacologists.

Mr. STOKES. We are very pleased to see Dr. Walker. He is a very distinguished editor.

Dr. LINDBERG. You are right. He and Dr. Spann filled up our conference room with an amazing group of people. We had an enthusiastic and very beneficial day of planning on how to activate this program.

Mr. STOKES. You worked with the nine other historically black colleges and universities?

Dr. LINDBERG. Yes. We took the opportunity to acquaint them with our toxicology information systems, so they got something out of the day as well. They are in a position to benefit their faculties and students and communities.

Mr. STOKES. I would appreciate it if you would put into the record the name of each of those HBCUs. Also, what level of funding supports this level of activity in the 1992 and 1993 budgets?

Dr. LINDBERG. If you want, I can name the schools or just put it in the record.

Mr. STOKES. You can put it in the record, but let's hear the funding that you have for 1992 and 1993.

[The information follows:]

HISTORICALLY BLACK COLLEGES AND UNIVERSITIES (HBCUs)

The nine HBCUs that are training medical and other health professionals in the use of toxicological, environmental, and occupational information resources developed at NLM are as follows:

Drew University School of Medicine—Madison, New Jersey
Morehouse School of Medicine—Atlanta, Georgia
Florida A & M University—Tallahassee, Florida
Howard University—Washington, D.C.
Meharry Medical College—Nashville, Tennessee
Texas Southern University—Houston, Texas
Tuskegee University—Alabama
University of Arkansas at Pine Bluff—Arkansas
Xavier University—New Orleans, LA

Dr. LINDBERG. Funding for the Toxicology Information Program is about $250,000. The amount of money planned for minority programs is closer to $830,000. We are also conducting an undergraduate research study program and there are access grants. There is a big project we have in mind, it is a lofty goal, and it is not in the funding, but that is the project Charles Walker introduced to us of a major effort in the delta.

When we met with representatives from the Delta Caucus, Mr. Espy, Mr. Thornton and the staff of Mr. Emerson from Missouri, I learned that the area is made of 217 counties in seven States. I must confess, I did not know that the delta was anything but the mouth of the Mississippi, but it is the lowlands along the river.

I remember when I was in Missouri, that Sikeston and Cape Girardeau and those areas were along the river, and were cotton country. But it seems that area is a very, very poor area. It is the country's Third World.

It made me think about our overseas project in Egypt. It made me wonder if we should not devote our attention to the delta region. We have enough money to have a conference which will either be in Memphis or Little Rock, depending on where it suits the people best, but we would like to come to understand who we can work with.

We, of course, know that there are four regional medical libraries involved in the Delta region. We have a unique project in Tutwiler, Mississippi. But we have to have amplifiers. We have to identify other organizations that will work with us and put their own efforts in it.

We are hoping that our planning conference will bring to light those people, and that we would be able to properly proceed with such an effort based on the outcome of that planning conference.

Mr. STOKES. Thank you very much, Dr. Lindberg.

Thank you, Mr. Chairman.

Mr. NATCHER. Mr. Early.

HIGH PERFORMANCE COMPUTING INITIATIVE

Mr. EARLY. Dr. Lindberg, I want to welcome you back to the Committee. I think that your graphics display really tells the story. The three examples show progress from 1989 to 1991. It makes me feel pretty good that this transfer is being achieved.

This past year the Library of Medicine lost a great friend in Jack Whitehead. And, I am happy to see Frances Howard here, who has done so much over the 17 years I have been on this Committee.

Does the NLM have a long-range or overarching plan for the high performance computing initiative?

Dr. LINDBERG. Yes, sir. We are believers in long-range planning, as you know. In the case of the high performance computer initiative, it is a national scheme, sponsored by OSTP, and now supported by Congressional legislation. The plan covers the period 1992 to 1997.

We are committed to be, so far as we are able, the biomedical participants in that plan. We think, as Mr. Natcher suggested, that our major contribution is biomedical applications, and helping those professions to know how to use it.

We are not going to say we cannot contribute something to the software programs as well. Our National Center for Biotechnology Information, in fact, already is. Our contribution, we think, would be in developing systems that let the biomedical profession know where things are, the electronic gateways, as they are called; and for the rest of it, I am perfectly happy for 85 or 90 percent of the money to come from Defense and Energy. That is okay with me, as long as we get a benefit.

Mr. EARLY. The budget request includes $18,800,000 for high performance computing and communications activities. How much have you allocated for grants and contracts to connect medical institutions to the high speed network, and how many awards do you expect to make?

Dr. LINDBERG. The numbers include a base line figure. When it started in 1991, we felt it was fair to say there was existing spending at $13,500,000 on areas related to HPCC. Excluding inflationary increases, the actual increment in money in FY 1992 is approximately $3,400,000.

Mr. EARLY. How many awards do you expect to make?

Dr. LINDBERG. The awards we are going to put up this year for hooking people up to it will amount to $1,400,000. We don't think that it will be necessarily through a grant program, but perhaps by a competitive contract program. $400,000 of those dollars we are going to spend through an agreement with the National Science Foundation. They have a very interesting outreach—they call it a connection program—which they have done with universities and colleges. We are going to ask them to include us and to add hospitals. They think that is a good deal and they would be willing to do that. So I guess we are piggy-backing a free ride there, too.

We will put up the money that goes to the hospitals, but they will do it, too.

Mr. EARLY. For the record, would you expand on how you are going to do that?

Dr. LINDBERG. Yes, sir.

[The information follows:]

CONNECTIONS PROGRAM

NLM through an Interagency Agreement with the National Science Foundation (NSF) will allocate $400,000 to enable medical institutions to connect to the NSFNET or Internet. Since 1986 the NSF has supported a program entitled "Connections to NSFNET" which provides grants to U.S. academic institutions to connect to the Internet. NSF has successfully managed this program and is willing to offer its staff and resources to administer NLM's funds for Internet connection grants to medical institutions including academic health centers, hospitals, and biomedical research institutes.

Such an agreement will expedite the issuance of these grants since NSF has an experienced staff and established expert panels to review the applications. Less lead time will thus be required to enable the medical institutions to gain access to the Internet.

NATIONAL NETWORK

Mr. EARLY. How many institutions do you plan to connect to the network?

Dr. LINDBERG. I don't know how the funding will be going for the next few years, but I would like to see NLM be told to get 100 or 150 top medical centers and hook them all up.

Mr. EARLY. How much money could you use for that? It doesn't make sense to have this knowledge and not disseminate it. That is where the Committee has always seen the importance of the Library of Medicine. You also plan to allocate funds to train scientists on the use of new computer capabilities. Could you give us an assessment of the manpower that you need in this area and the number of scientists that should be trained?

Dr. LINDBERG. We think the best way to do it is to continue or increase the number of slots in the authorized training programs. There are 10 programs that have been recompeted and reselected. In fact, there is money in the budget for this training initiative of about $400,000, but I cannot spend it to solve this training problem because of the MLAA cap. It would really be advantageous to transfer the monies that exist to the training function.

UNAUTHORIZED PROGRAMS

Mr. EARLY. Why is it that you cannot spend it?

Dr. LINDBERG. The programs not reauthorized were capped at the 1991 level.

Mr. EARLY. Would you list those for the record, too?

Dr. LINDBERG. Yes, sir.

[The information follows:]

UNAUTHORIZED PROGRAMS

The unauthorized programs frozen at the FY 1991 level are as follows:

(1) Medical Library Assistance Act (MLAA)—includes those extramural programs of Resource, RMLs, Training and Fellowships, and IAIMS. Additionally, the planned

expansion of the High Performance Computing and Communications (HPCC) and Outreach initiatives using the extramural mechanism was eliminated.

(2) Biotechnology—includes the National Center for Biotechnology Information and extramural biotechnology grants, plus Toxicology Information's biotechnology database.

NATIONAL CENTER FOR BIOTECHNOLOGY INFORMATION

Mr. EARLY. What is the Biotechnology Center's role in the high performance computing initiative?

Dr. LINDBERG. We plan for them to have a prominent role. We would put about $1,000,000 a year into the National Center for Biotechnology Information based on a good plan and good performance. The task that they have to do, Mr. Early, is to take the sequence data. This is GenBank, Protein Identification Resources, Swiss Prot, all the different data bases, U.S. and international, and put them together in a synthesized database so that they make sense taken together. They are being put together in a number of forms and formats that are available to American scientists.

One is through a CD-ROM. These disks are amazing. They are designed to play music, but you can put text on them as we do with the UMLS or the sequence data. These are distributed on an experimental basis now. They have programs with them because in the new world of computer data bases, the data base is no good unless you have a program to read it.

Dr. David Lipman has gone beyond that now and linked the gene data with the Medline data. That is the scientific papers that the gene references. There is now a conceptual extension beyond this step too. One can get sequences that are "like" the ones he specifies and one can ask for papers that are "like" those that reported the sequences. Then there is a double linkage.

Mr. EARLY. Is that how we disseminate the information we have available on molecular genetics to the academic and private sectors?

Dr. LINDBERG. That is right. They have the option to get mailed one of these and do it on their own computer or to use the NREN, the high speed network.

Mr. EARLY. Both sectors have what they need?

Dr. LINDBERG. We think that most scientists have what they need. The smaller universities and all the hospitals may not, but right at the moment, the scientists really have what they need and they have a choice of doing it locally or calling up the network and doing it in on-line.

GRATEFUL MED

Mr. EARLY. A cornerstone of your dissemination system is the Grateful Med. How many physicians and other health professionals have been trained in this system?

Dr. LINDBERG. We have sold or provided through NTIS copies to about 50,000 health professionals. In the last year, we actually have trained some 3,000 through these outreach contracts. It is unknown exactly how much training you really need. As you know, you buy things all the time and they say it is so simple, a child can assemble it. We claim our programs are so nice almost anybody can operate them right away but it helps to have somebody start you out right.

We do know that an increasing number of people use Grateful Med. It is not just the younger people, although recent graduates do tend to use it. People can use it on IBM machines or the MAC computers. It has increased 44 percent in the last year. So by and large, we are reasonably happy with that.

Mr. Early. Does lack of resources preclude you from training more professionals?

Dr. Lindberg. I think outreach can always use more money. Outreach is a people-intensive thing. Those are things that we do through the National Network of Libraries of Medicine. That involves people going out into the community and giving courses.

Mr. Early. I think that this is where we should be going with the computer network, not only at the Library, but also at the State Department, Customs, et cetera. From your presentation, the library seems to be doing it pretty well. I have a lot more questions which I will come back to on the next round. I want to thank you very much.

Dr. Lindberg. Thank you very much.

BASIC LIBRARY SERVICES

Mr. Natcher. Now, Doctor, with the emphasis given in recent years to special initiatives like outreach and biotechnology, have sufficient resources been allocated to basic services?

Dr. Lindberg. I regret to say that, for a variety of reasons, we have fallen behind somewhat on basic library services, partly because of the necessary reductions that have had to come because of the budget caps. You know, we don't decrease earmarked funds, so the reductions have to come out of whatever else is there, and that is usually library operations.

There is also the increase in work. There is more knowledge, more books, more journals, more reports and users. That falls hard on our library operations' people. That is about two-thirds of our budget.

So we are about $2,000,000 below where we ought to be in terms of current services and $3,000,000 below where we would be doing a good job. It is the inadvertent consequence of the means of budget balancing plus the increased volume of information.

Mr. Natcher. When do you expect to run out of library shelf space?

Dr. Lindberg. We think we are okay until 2002 if we can purchase some additional compact shelving. When I came, they told me it was 2020, but I guess everything is growing faster than expected. But, at any rate, it is not next year.

We use the systems called compact shelving where the shelves slide together. It is solid books and then, the motorized shelves slide open. We have not been able to get any in the last two or three years. This is a temporary acute problem, and there won't be any bigger problem until 2003.

LITERATURE ACQUISITION

The CHAIRMAN. What are you budgeting for library acquisition costs in 1993? How does this compare to previous years?

Dr. LINDBERG. The 1993 President's budget is $5,458,000. That is about 10 percent above the 1992 estimate. I cannot guarantee that will get 10 percent more books and journals. The cost of these materials inflates faster than the cost of living.

Mr. NATCHER. What is the minimum amount of acquisition you think you should be doing each year?

Dr. LINDBERG. I think this number is suitable. We are not skimping at that number.

PRESERVATION PROGRAM

Mr. NATCHER. Last year you microfilmed 2,000,000 pages of documents in your preservation program. How much more remains to be done?

Dr. LINDBERG. That is a bit of a disappointment for me. You and the Committee have helped us, Mr. Natcher, and recognized the importance of preservation.

In 1985 we estimated that 8 percent or 35,000,000 pages were brittle. You could read them once or copy them, but then they would fall to pieces. You could only do one thing. I regret I had no choice but to undertake to microfilm them. It would be wonderful to put them in a computer, but it is not cost-effective. We later determined that 11 percent of the collection, or closer to 60,000,000 pages were brittle.

In 1992 we will complete 24,500,000 pages of microfilming—so 40 percent of that is done.

It is getting smaller even though it is not getting smaller as fast as I wanted it to.

CATALOGING BACKLOG

Mr. NATCHER. What is the current size of your cataloging backlog and what do you project for 1993?

Dr. LINDBERG. That is also a disappointing story. In FY 1991 the backlog was down to 10,000 but it will climb up to 21,000 if we are not careful. That is because, as I indicated, the basic services are underfunded in our budget this year. We are adopting by fully funding indexing, the purchase of journals etc., and processing, including interlibrary loans. These are things that users see right away.

We have to cut back someplace. Cataloging is one of the places we are cutting back. That is too bad, but it gives us a little elbow room and creates a long term problem rather than a crisis. The backlog in cataloging will most assuredly grow.

But I must say, about the percentage of pages growing brittle, I should tell you that in the world of university libraries there have been studies by Princeton, Columbia and Harvard, and their estimates of the percentage of brittle pages run from 17 percent to 33 percent.

So biomedical libraries, even though they are 11 percent brittle, are far better off than general libraries. I am not sure why. Maybe we take better care of them or they are on coated paper. I am not sure.

We are more fortunate than the general library in that respect.

COMPUTER CAPACITY

Mr. Natcher. Are the mainframe computers that operate your data bases running at close to capacity?

Dr. Lindberg. They once again are. We have actually been able to predict fairly well when we need the machines because the work load increases from 15 to 18 percent a year. While the computer operation, per se, gets more efficient, the number of users is increasing faster.

We have just gotten a new machine. It was acquired last year. It is now installed and ready. Within the next year we simply have to go to another doubling. We are going to need $2,000,000 for one more upgrade.

I think when this upgrade needs replacement, we will be into a totally different hardware architecture. I think the world of information retrieval has changed radically and we will be down to where decisions will not be multi-million-dollar decisions. I think they are going to be smaller, and that will be more comfortable.

PUBLICITY

Mr. Natcher. Doctor, how much do you spend each year on publicizing the library's products and services that are offered?

Dr. Lindberg. We budgeted about $500,000 this year with hopefully $1,000,000 in FY 1993. Of course, it is not spent in taking out advertisements in the newspapers as somebody would if it was a business. But it is spent through outreach efforts, largely through the efforts of the exhibitions at scientific meetings. Then, too, we cannot do them all ourselves, but the regional medical library people help us. We have been able to increase from 25 to 45 this year. That is possible only with regional help.

A program we are starting with the Maine Biological Laboratory in Woods Hole, Massachusetts, this year is a scientific counterpart to the outreach. For five years we have assisted at FASEB meetings, for young American scientists, some in Vermont, some in Colorado. In our outreach we must concentrate on scientists as well as practitioners.

We have a modest investment with the Woods Hole people to conduct a course in medical information and set up a computer resource so that all the scientists who come to that institution have an opportunity to see the data bases and to take short courses in their use.

We contributed some money to a PBS film called, The Future of Medicine, as did other NIH institutes as well.

We have looked into the matter of getting help from a firm to do more outreach and even a publication. We have not funded that as yet. We are not sure we are going to be able to afford it this year. That is one thing we hope to do as soon as that is feasible.

IAIMS

Mr. NATCHER. For how many years will current IAIMS grantees receive support?

Dr. LINDBERG. At present, we are funding nine programs, and all of those would be over in three years. The amazing thing, Mr. Natcher, is that we kind of promised the Congress that we could see through to the end for Phase 3 IAIMS. That will be done in three years.

The schools are intrigued by the program. We continue to get requests even for Phase 1 which are small grants, $100,000 a year, even from schools who know they probably will not be able to fund them but they compete vigorously. There are five approved ones right now. In total, we funded 17 schools, and there were another 17 that were approved but unfunded. The schools are enthusiastic about it.

Mr. NATCHER. Do you plan to award any more new Phase 1 IAIMS grants in 1993 or later years?

Dr. LINDBERG. There are five approved schools, so we would like to be able to do that if recycling the money is necessary, but there are no funds available to do that in the next year.

SMALL HOSPITAL LIBRARIES

Mr. NATCHER. Are you changing the focus of your Medical Library resource grants to emphasize smaller hospital libraries?

Dr. LINDBERG. Yes, sir. We are. I think it is regrettably true that while we claim that we do a very good job with the universities and sophisticated libraries, we never felt we did an adequate job with the small hospital libraries. There are thousands to start with. We have refocused that program in the hopes that we can do better for them.

One of the new aspects, actually, is to try to get some help for small hospitals in the writing of proposals. Some of the people we want to help are reluctant to turn in a research grant. We are trying to devise a scheme whereby the regional libraries will help the smaller institutions to get in the act to start writing proposals.

Mr. NATCHER. Mr. Early?

CATALOGING BACKLOG

Mr. EARLY. Thank you, Mr. Chairman.

In the area of cataloging, Doctor, you told the Chairman that the backlog was below 10,000 but that it is going to increase to 21,000. Is there a better approach to cataloging that we could be using?

Dr. LINDBERG. Actually, the worst we have ever been was in 1981. I came in 1984. I was somewhat appalled by this problem. First of all, it seems like it is intellectually more difficult to index an article than it is to catalog a book, but the reverse is true.

We spend more money cataloging some books than we do buying them. That seems amazing. You might attempt to simply quit doing it. But we catalog it, nobody else has to. Because all the other medical libraries in the world use that catalog information, we have an obligation to do it and to do it right.

The country is committed to the so-called Anglo-American cataloging rules. I think they may be too complicated, but that is what everyone has agreed to. How can we make the things more efficient? We now use computers to look up words and help a person choose them instead of typing them. That was a big help.

We actually have unfilled cataloging positions. Even when there was a tight lid on FTEs on cataloging, we had trouble getting good people. How to do better than that? One answer is a thing I think NIH does a very good job at, and that is the flexible workplace arrangement.

I was appalled to see in the Wall Street Journal this week somebody lambasting the Federal Government for doing a terrible job in that. I think the reverse is the case, particularly at the NLM where we have demonstrated that someone can work at home and still be properly supervised.

The Library has been a leader in using this approach. We think that will help us, but we are underfunding the problem, because we are robbing Peter to pay Paul.

Mr. EARLY. Why don't you expand on that for the record—where you think NLM is doing a good job with regard to flexible workplace.

[The information follows:]

FLEXIBLE WORKPLACE

NLM was among the first NIH components to participate in pilot tests of the flexiplace program first in 1986 and again in 1991. The Library now has more than 13 employees participating in the program. Most of these are NLM indexers and catalogers who work at home several days a week, coming to the Library at least two days to be available for consultation with supervisors, attend meetings, etc. Both indexing and cataloging lend themselves to this arrangement because employees can use the same online indexing and cataloging systems from their homes and their productivity while working away from the Library is easily measured. NLM supplies the computer equipment and communication lines needed. Employees who participate in the program maintain or improve the quality and quantity of their work while working at home. The participants are strongly in favor of the program. It eliminates lengthy commuting several days a week; it enables less expensive daycare arrangements; and for employees with significant impaired mobility, it makes working much less physically exhausting. NLM sees the availability to the flexiplace options as a powerful tool for recruiting and retaining good employees. The program appears to be particularly attractive to working women.

Mr. NATCHER. Dr. Lindberg, we want to thank you and your associates for appearing before our Committee at this time on behalf of your budget request for 1993. It has been a good hearing. We thank you.

We will adjourn until 10:00 in the morning.

[The following questions were submitted to be answered for the record:]

Resource Grants

Mr. Natcher: Is there a financial need component to applications for medical library resource grants?

Dr. Lindberg: Yes. The Resource program, which is designed to provide assistance to medical libraries in acquiring or upgrading computer and telecommunication technology, was created largely because NLM is aware that libraries, particularly small hospital libraries, commonly have great difficulty in acquiring sufficient resources from their parent institutions. NLM's review procedure pays particular attention to the applicant's needs, current technological status, the availability of alternate funding sources, and the likelihood that the grant would make a significant difference. The medical libraries which apply for resource grants would not in most instances be able to carry out their projects without NLM support. The need for NLM help is particularly clear in applications from medical libraries which respond to our announced goal of encouraging proposals to help underserved health professionals in rural and inner city areas.

Unified Medical Language System

Mr. Natcher: When will the Unified Medical Language System be completed?

Dr. Lindberg: When Congress first increased NLM's appropriation to support the Unified Medical Language System (UMLS) in FY 1986, we estimated that it would take at least 10 years to develop the basic components of the system and to make them available in automated systems used by health professionals and researchers throughout the United States. Based on progress to date this timetable still seems reasonable. After FY 1996, there will be ongoing maintenance costs to keep the UMLS current with developments in biomedicine; i.e., to add new concepts and to provide automated referral to new sources of machine-readable information. This requirement for ongoing support is analogous to continuing resource requirements for other NLM products and services such as the MEDLINE database.

Training Fellowships

Mr. Natcher: Describe your new research training fellowships in Informatics. How many fellows are you supporting in 1992 and 1993?

Dr. Lindberg: The training emphasizes synthesis, organization, retrieval, and effective management of knowledge. It will be inter-disciplinary involving medicine and the biological sciences, the cognitive sciences, information science, and computer science. The training sites offer university graduate course work and opportunities for meaningful trainee involvement in health computer science research.

NLM has funds to support 77 trainees in FY 1992 and 85 trainees in FY 1993. In addition to training grants, NLM will support about 8 individual fellows in FY 1992 and FY 1993.

NLM Reimbursements

Mr. Natcher: Identify the sources of your expected $16.1 million in 1993 reimbursements.

Dr. Lindberg: The primary organizations providing funds to the NLM are the Health Care Financing Administration, Department of Commerce, Agency for Toxic Substances and Disease Registry, Environmental Protection Agency, and Agency for Health Care Policy and Research. These funds will provide data communication services through NLM's Value-Added Network (VAN) contracts with TYMNET, TELENET, and CompuServe which provide telecommunications capabilities; provide support for NLM's online services, machine readable products, and document delivery service; provide support and maintain the activities of NLM's toxicology information databases; and provide support for the information center (Office of Health Services Research Information) at NLM on health care technologies and health care technology assessment.

High Performance Computing and IAIMS Funding

Mr. Natcher: What is your 1992-1993 funding for (a) high performance computing and (b) IAIMS?

Dr. Lindberg: NLM's funding for high performance computing and IAIMS is as follows:

	FY 1992	FY 1993
High Performance Computing	$3.375 million	$4.253 million
IAIMS	$3.995 million	$4.143 million

Extramural Grants

Mr. Natcher: Provide a mechanism table for extramural grants by type of program (e.g., biotechnology, IAIMS, etc.).

Dr. Lindberg: The breakout of extramural funding for FY 1992 and FY 1993 is as follows:

	(dollars in thousands)	
Extramural Program	FY 1992 Estimated	FY 1993 Estimated
MLAA		
IAIMS	$3,995	$4,143
Resources	1,237	1,179
Lib. Info. Sci.	211	256
Training & Fel.	3,428	3,612
Publications	320	341
RML Contracts	5,500	5,704
Total, MLAA	$14,691	$15,235

Medical Informatics		
Research	$7,377	$7,766
Biotechnology	3,991	4,179
Total, MI	$11,368	$11,945
Total, Extramural	$26,059	$27,180

Outreach and High Performance Computing Budget

Mr. Natcher: Break out the budget for outreach and high performance computing by program for 1992 and 1993.

Dr. Lindberg: The breakout of outreach and high performance computing funding for FY 1992 and FY 1993 is as follows:

	(dollars in thousands) FY 1992 Estimated	FY 1993 Estimated
EXTRAMURAL:		
MLAA		
RMLs		
Outreach	$2,799	$2,902
High Performance Computing	0	
Resources-Networks		
Outreach	732	759
High Performance Computing	0	0
Training & Fel.		
Outreach	502	520
High Performance Computing	0	0
IAIMS		
Outreach	500	519
High Performance Computing	0	0
Total, Extramural		
Outreach	4,533	4,700
High Performance Computing	0	0
INTRAMURAL:		
Library Operations		
Outreach	1,939	2,011
High Performance Computing	0	0
Lister Hill Center		
Outreach	0	0
High Performance Computing	2,875	3,734
Biotechnology Information		
Outreach	0	0
High Performance Computing	500	519
Total, Intramural		
Outreach	1,939	2,011
High Performance Computing	3,375	4,253
NLM Total:		
Outreach	$6,472	$6,711
High Performance Computing	$3,375	$4,253

IAIMS Grants

Mr. Natcher: Do medical schools use IAIMS grants to buy computer hardware?

Dr. Lindberg: No, IAIMS funding supports only a small core group of individuals responsible for the planning and development of IAIMS. NLM's IAIMS grants provide only a small proportion of the total costs involved, between 10 and 20 percent. Institutional contributions for the remaining costs include computer hardware purchases.

Research Training

Mr. Natcher: Are you considering submitting a reprogramming proposal to shift additional funding into research training? Why would such a shift be desirable?

Dr. Lindberg: Yes, a reprogramming request is under consideration. NLM fully recognizes the need for practical application of modern developments in medical informatics, but also is aware of the extraordinary importance of ensuring that the nation has a cadre of scientists who can continue the basic and applied research which must be done in this new field of medical informatics. If we are to realize the potential for biomedicine of the remarkably rapid advances in information technology, we must foster the appropriate skills and knowledge. For example, the High Performance Computing and Communications initiative (HPCC) requires an intense research effort if all the technological power being developed is to be usefully applied to such health-related issues as efficient transmission of MRI images, real-time analysis of radiological cancer treatment options, networking of molecular biology research, hypermedia education systems and others.

The mandatory freeze of MLAA funds for FY 1992 at FY 1991 levels eliminated approximately 12% of the trainees we had planned to support through our institutional training programs, a loss we can ill afford in a field which urgently needs expansion. Reprogramming could, at the very least, permit use of this otherwise wasted training capacity.

Health Services Researchers

Mr. Natcher: The Institute of Medicine has issued a report on information needs of health services researchers. How close are you to meeting the Institute's recommended standards?

Dr. Lindberg: The Institute of Medicine submitted a report to NLM on "Improving Information Services for Health Services Researchers" in September 1991. The report recommends that the Library take action: (1) to improve access to the literature of health services research, including practice guidelines, regulations and policy documents; (2) to provide automated access to other information important to health services researchers, including research in progress and data sets available for use in health services research; (3) to improve the ability of librarians within the National Network of Libraries of Medicine (NN/LM) to handle complex health services research inquiries; (4) to expand the Unified Medical Language System® (UMLS®) to improve its utility in encoding, retrieving, and analyzing health services research data; and (5) to promote the use of current and emerging NLM and NN/LM services among producers and users of health services research information.

In December 1989, NLM received a congressional mandate to work with the new Agency for Health Care Policy and Research (AHCPR) to improve the organization and dissemination of health services research information. In the past two years, NLM has taken a number of steps to carry out this mandate, including establishing a new Office of Health Services Research Information, improving the Medical Subject Headings (MeSH) vocabulary to facilitate indexing and retrieval of health services literature including practice guidelines, enhancing NLM's collection of health services research literature, adding information about relevant organizations to the DIRLINE (Directory of Information Resources) file, initiating the development of new databases related to health services research, and beginning to publicize NLM's products and services to health services researchers. These activities are compatible with the IOM recommendations, but it will take another five or six years for NLM to achieve the level of service outlined in the IOM report.

Mr. Natcher: Can you estimate the cost of the Institute's recommendations?

Dr. Lindberg: The IOM report recommends a health services research information budget of about $3 million dollars for FY 1993 and about $2 million dollars each year for the subsequent 5 years.

Products or Databases Competition

Mr. Natcher: Do you have any competition from the private sector for your products or databases?

Dr. Lindberg: No, private sector providers are encouraged to develop value added products and services. The National Library of Medicine (NLM) licenses its databases to private sector organizations as part of a broad strategy to make the Library's authoritative data available as widely as possible to health care practitioners and researchers. As a result of NLM's policy, several commercial database vendors and a growing number of educational institutions lease NLM data and in turn make it available to customers or institutional affiliates. Through the use of special experimental agreements, NLM facilitated the development of a number of private sector CD-ROM products, which provide another alternative for access to NLM data, often in institutional settings. NLM itself has developed Grateful Med®, an inexpensive personal computer software package, to provide an easy, low-cost way for individual health professionals to conduct basic searches of NLM's databases. Grateful Med is an important component of NLM's Outreach Program which is designed to increase awareness and use of NLM's products and services, particularly among health professionals in rural and inner city areas.

Scientific Information Dissemination

Mr. Obey: NLM's mission is to aid in the dissemination of scientific information important to the progress in medicine. How do NLM's policies requiring the payment of royalties and imposing restrictions on redissemination further this mission?

Dr. Lindberg: NLM's pricing policy and distribution mechanisms have been reviewed by DHHS, OTA and GAO in the past and have been approved by the Appropriations Committee as providing a good balance among competing "goods"; i.e., broad access to high quality biomedical information and economic competition. They also help contain the cost of government, since these activities presently generate $13 million in access costs that are currently distributed among users of MEDLARS data.

NLM establishes charges for use of its machine-readable databases in accordance with a pricing policy established by its Board of Regents and endorsed by the U.S. Congress. This policy requires NLM to recover the incremental cost of access to its data, but not the basic data creation costs; e.g., acquisition of literature, indexing, cataloging, etc. These latter costs are considered part of NLM's basic library services and are paid from NLM's appropriation. At the specific guidance of the Congress foreign users pay a surcharge to cover their proportionate share of data creation costs because they are not contributors to the tax revenue used for NLM's appropriation. Access costs that are unique to one method of access are paid for only by the users of that method; e.g., telecommunications costs are figured into the charges to online users only. Costs incurred to make the data available in any machine-readable form are spread across all users irrespective of their method of access to the data, whether online to the NLM system, online to commercial or university systems that lease data from NLM, or via commercially produced CD-ROM products. By distributing such costs equitably among the very large number of users of MEDLARS data, NLM ensures that the charges to individual users are low.

The current policies have been very successful in ensuring broad low-cost access to NLM's data. As measured by online connect hours, use of NLM's data throughout the world has nearly doubled since FY 1987 to a total of 1.2 million connect hours in FY 1991. Use of NLM's own online system accounts for about 28% of these online connect hours. The remaining usage is on systems provided by commercial companies, universities, and the International MEDLARS centers. The connect hour figure excludes use of NLM's data on CD-ROM products. There are more than 8,000 subscribers to the several commercially available CD-ROM products that include NLM data. The number of licensees receiving NLM data and redistributing them has grown 85% in the past five years.

NLM imposes some restrictions on the redistribution of its data in order to ensure that (1) updates and corrections to the data are made available to all MEDLARS users (2) distributors describe the NLM data in their products accurately, e.g. in terms of publications years or subsets of journals covered, and (3) software provided for use of NLM data performs reliably, e.g. all the included data indexed by a particular subject heading is retrieved when that heading is searched. NLM adds information to its databases weekly, annotates existing records to highlight articles for which subsequent retractions, error notices or substantive comments have been published; and corrects any indexing errors that may impair retrieval of relevant material. There have been a number of cases when incorrect drug dosages have been published in abstracts and therefore entered in NLM databases. It is critical that such errors be flagged and corrected for all users of NLM's data as quickly as possible.

Mr. Obey: Wouldn't lower prices and greater distribution of NLM information be more consistent with the statutory dissemination goal?

Dr. Lindberg: NLM's current pricing and distribution policies have ensured a variety of very low-cost options for searching NLM's data, with an average cost per search of a few dollars or less, and have also supported dramatic growth in the number of people who have ready access to the data. These policies appear to be entirely consistent with the goal of broad dissemination of scientific information. They also ensure that the information available is accurate and up-to-date.

Mr. Obey: Will the development of end user software by NLM interfere with the existing private market for such software?

Dr. Lindberg: NLM introduced the Grateful Med end user software package for searching the databases on the NLM online system in 1986 after determining that such a product was not available. Since that time more than 40,000 copies of the software have been sold with the majority purchased by individual physicians. In the same five year period, a number of commercial firms have developed and successfully marketed CD-ROM products providing access to NLM's data and more than 40 institutions have mounted portions of NLM databases for online use within their institutions. In addition to providing direct online access to many U.S. health professionals, Grateful Med appears to have raised the general level of interest in end user searching, thus increasing the market, and to have fostered the development of a number of alternative ways to provide such access.

Mr. Obey: Has NLM conducted a study to determine that its participation in the market for end user software will be beneficial or detrimental?

Dr. Lindberg: NLM has not conducted such a study, but the actual experience of the last five years appears to indicate that NLM's participation in the market has been beneficial. Health professionals now have a greatly increased set of low cost options for access to NLM's data.

Mr. Obey: Currently the NLM has a redistribution policy which requires the licensing of distributed data and the collection of royalties. Will these restrictions apply to the National Center for Biotechnology Information's (NCBI) distribution of DNA data?

Dr. Lindberg: Biological sequence information has become a critical and widely used resource for biomedical research. A major reason for this has been the consistent policy of unrestricted access to federally funded sequence databases. NCBI will continue this policy and distribute all molecular biology data without restrictions unless that data comes from a source which imposes its own restrictions on distribution. The DNA and amino acid sequence data will therefore be distributed without restrictions.

Mr. Obey: Will these restrictions apply to the Medline data that NCBI may distribute along with the DNA data?

Dr. Lindberg: As stated above, biological sequence data from federally funded databases has always been distributed without restrictions on use and redistribution. Furthermore, a major source of this information to the databases is direct submission of the data by authors. Given this context, the National Library of Medicine (NLM) has decided to make available without restrictions those Medline records which directly link to sequence database records, or which carry the "Molecular Sequence Data" MeSH term. The current Medline licensing policies will still apply to those Medline records which are not members of this "Sequence Subset".

Mr. Obey: Would these restrictions apply if a vendor of DNA data does not use the exact Medline references used by NLM in its own information products?

Dr. Lindberg: Medline records which are members of the "Sequence Subset" as defined above may be distributed without restrictions. The current Medline licensing policies will still apply to those Medline records which are not members of this "Sequence Subset".

Mr. Obey: The National Institute of General Medical Sciences in its distribution of Genbank data since 1982 relied upon private initiatives to develop end user software to be used with the Genbank data, the NCBI will now be distributing Genbank data and has departed from this approach by deciding to develop end user software as well. Why is it necessary for the NCBI to develop end user software?

Dr. Lindberg: NIH has always supported both the creation of molecular biology databases as well as the development of software tools for managing and analyzing this data. Examples include the PROPHET system at Bolt Beranek and Newman, the Protein Identification Resource at the National Biomedical Research Foundation, and hundreds of grants to developers of computational tools for sequence analysis. Even the current Genbank contract allocates significant resources for end user software such as

Authorin, a package for creating entries to submit to the database, and the GenBank relational database system which is set up at a number of satellite nodes for distribution and retrieval of Genbank information. NCBI is continuing this policy of developing databases and softwares tools for analysis and retrieval of sequence information. Computational tools developed at NCBI have been central to the identification and analysis of the genes for Neurofibromatosis ("Elephant Man's Disease"), familial colon cancer, and Kallman Syndrome. The source code for all software developed at NCBI is available without restriction, and a number of developers have participated in workshops on the use of these software libraries and are working to incorporate this code in their commercial products.

Mr. Obey: What is the estimated total cost of developing GENINFO, including charges by NTIS and NLM for related services?

Dr. Lindberg: GENINFO is the term used to describe an integrated set of sequence databases that NCBI will distribute. The major component for which NCBI is responsible is the GenBank Nucleotide sequence database. GenBank will be produced through an Interagency Agreement with Los Alamos National Laboratory who will process the direct author submissions and the NLM's Library Operations Division which will create records from the journal literature. A contractor is used for the keyboarding of the sequences from the journal articles. Finally, computer analysts and programmers within NCBI are responsible for the overall design of the system, maintaining the data entry/data exchange software, and incorporating other public sequence databases (e.g., EMBL, PIR, Swiss-Prot) into the system. Development costs which are financed in FY 1992 include:

$335,000	NLM Sequence Indexers
$195,000	Sequence Keyboarding
$158,760	Software Design & Development
$688,760	Development costs - FY 92

Mr. Obey: What is the estimated total cost of operating GENINFO, including charges by NTIS and NLM for related services?

Dr. Lindberg: For the operation of the database, beginning in October, 1992 there will costs similar to that for the design and testing phase for the salaries and benefits for the NLM sequence indexers and the keyboarding contract. The costs for the software design component will be replaced by a software maintenance and production component. The processing of sequence submissions will continue to be performed by Los Alamos through an Interagency agreement. Distribution of the data will be through the Government Printing Office. Users will pay for the cost of the subscription service; NCBI will pay only for the cost of mastering the CD-ROMs. Below are estimated annual costs for operating GENINFO beginning in October, 1992.

It is important to note that for the costs outlined below, the content and scope of the database will be increased over that of the current GenBank project. The NLM scanning of journal articles will add a significant literature component to the database in addition to the capture of protein as well as DNA sequences. Furthermore, through an R&D contract mechanism, known as a Broad Agency Announcement BAA), support will be provided to the academic and commercial sector to become active collaborators in enhancements to the database by adding specialized biological knowledge to the sequence records.

$ 351,750	NLM Sequence Indexers
204,750	Sequence Keyboarding
214,987	Software Maintenance and Support
320,000	Computer Hardware and Software Maintenance
2,400,000	Direct Submission Processing
28,200	CD-ROM mastering charges
500,000	R & D for Database Enhancement
$4,019,687	Annual Projected Total - FY 93

Mr. Obey: What is NCBI's annual projected cost of operating GENINFO?

Dr. Lindberg: As outlined above, $4,019,687 is the estimated amount of annual operating cost.

Mr. Obey: Please provide a table which includes NLM funding levels and FTE's over the past 10 years and the NCBI funding and its FTE's since its inception.

Dr. Lindberg: The statistics are as follows:

National Library of Medicine

Year	Appropriation	FTE
1983	$51,943,000	495
1984	49,613,000	544
1985	55,910,000	531
1986	55,322,000	501
1987	61,838,000	510
1988	67,910,000	510
1989	73,731,000	511

Year	Appropriation	FTE
1990	81,861,000	550
1991	91,407,000	585
1992	99,323,000	613
1993	108,663,000	613
	National Center for Biotechnology Information	
1989	4,764,000	12
1990	5,023,000	22
1991	5,777,000	27
1992	7,014,000	34
1993	10,767,000	34

Mr. Obey: Please include job descriptions and salaries of the NCBI staff in FY 92 and FY 93 request.

Dr. Lindberg: The information is as follows:

Position Title	Salary
Director, NCBI	$108,078
Computer Specialist	83,502
Visiting Scientist	79,200
Visiting Scientist	76,465
Computer Scientist	72,797
Research Medical Officer	72,024
Medical Officer	69,167
Research Biologist	60,070
Visiting Scientist	57,490
Computer Specialist	56,990
Operations Research Analyst	56,990
Visiting Associate	56,406
Computer Scientist	55,450
Senior Medical Staff Fellow	54,833
Visiting Scientist	53,760
Operations Research Analyst	52,370
Computer Scientist	52,370
Research Biologist	50,830
Research Biologist	50,830
Computer Scientist	47,750
Research Biologist	46,210
Senior Staff Fellow	42,019
Administrative Officer	41,451
Staff Fellow	41,219
Staff Fellow	40,895
Computer Specialist	38,861
Visiting Scientist	38,860
Staff Fellow	38,648
Staff Fellow	37,523
Operations Research Analyst	32,423
Visiting Fellow	31,260
Visiting Fellow	29,332

Visiting Fellow	26,356
Visiting Fellow	26,230
Secretary (Typing)	24,826
Secretary (Typing)	22,998
Clerk (Typing) SIS	17,916
Clerk (Typing) SIS	17,916
Computer Scientist	17,686
Clerk (Typing) SIS	16,896

Mr. Obey: How much has been spent through FY 92 for developing end user software to be used with GenBank data?

Dr. Lindberg: Through FY 92, NCBI has committed approximately 2.5 FTEs for the development specifically of the Entrez end user software. This cost is approximately $126,000.

Mr. Obey: How much is requested in the FY 93 request for developing end user software?

Dr. Lindberg: For FY 93, NCBI is requesting approximately $132,300 for the development and support of the Entrez end user software and Blast network sequence search software.

Hospital Access

Mr. Stokes: I understand that information resources at a national and international level are growing at a faster rate than the ability of local medical libraries and other facilities to use them. To what extent is this a problem? Are certain medical facilities in danger of being isolated from the growing national information capability?

Dr. Lindberg: The problem is already bad, and will get worse as the volume of publications increases and the cost of journals continues to soar. Even major medical center libraries are cutting back on their subscription list because of the sheer expense of acquiring and maintaining a modern collection; many smaller hospital libraries can no longer maintain even a good core collection for direct clinical application, and the health workers associated with such facilities will find it increasingly difficult to obtain appropriate information quickly and efficiently.

Mr. Stokes: How is the Library addressing this issue?

Dr. Lindberg: The only feasible solution is development of national telecommunication networks through which all can gain access to the entire body of relevant literature as it is stored at one or more central reference libraries. The development of such a network, and facilitation of access to it for all are prime goals of NLM. The national network concept is clearly the key whether journals remain largely a print medium or evolve eventually into electronic form.

Specific extramural programs used by NLM for this purpose include resource grants to hospital libraries and medical center libraries to improve their computer and telecommunication capabilities, demonstration projects which will apply high performance computing and high performance digitized communications for the solution of a significant problem in a biomedical domain, and a project utilizing a National Science Foundation agreement to support a connections program.

Mr. Stokes: What level of funding will be used to support these activities in FY 1993? How does this compare to FY 1992?

Dr. Lindberg: The FY 1993 budget provides $2,500,000 to support these activities. The FY 1992 budget provides $3,000,000.

Training

Mr. Stokes: I also understand that there are not adequate numbers of persons in the biomedical fields who have had training in the use of modern computer and communications systems. To what extent is this a problem?

Dr. Lindberg: The problem is serious, and limiting significantly the ability of institutions to modernize their information systems. The shortage of managerial-level professionals who can advise CEO's about the expensive, highly complex decisions which must be made is proving to be a major bottle-neck. The issue cannot be resolved simply by purchasing some off-the-shelf system. None exist, and in any event, most institutions already have a heavy investment in some mixture of components and systems. What is needed is sophisticated help in achieving an integrated system without scrapping what has already been purchased and installed.

Mr. Stokes: Are major university medical centers having difficulty recruiting senior professionals in this area?

Dr. Lindberg: Finding sophisticated senior people is difficult, and there are many current vacant positions for which active recruitment is going on. At the moment we are seeing a good deal of raiding: people who know how to plan, implement, and administer modern information systems are recruited away from other campuses, which, of course, merely transfers the problem from one site to another.

Mr. Stokes: What activities are you supporting in this area?

Dr. Lindberg: We have an important training initiative in informatics research, but recognize the need to provide an adequate supply of trained professionals capable of applying informatics to meet the needs of medical centers. Our IAIMS program, which is designed to integrate information systems at medical centers, has produced a number of experienced administrators who are highly sought-after. Even the junior members of an IAIMS team are often heavily recruited. To supplement the IAIMS program, NLM introduced during FY 1992 a new Fellowship in Applied Informatics which is open to all health professionals, and which is specifically designed to augment the number of those expert in the use of computer and communication systems. It is too early to comment on the utility of the fellowship program.

Mr. Stokes: What level of funding will be provided in FY 1993? How does this compare to FY 1992?

Dr. Lindberg: The FY 1993 budget provides $148,000 for the fellowship program. ($308,000 was available in FY 1992).

Toxicology Initiatives

Mr. Stokes: A Long Range Planning Panel on Toxicology and the Environment was created in 1991 to access the Library's toxicology related information services and advise on their future direction. What activities are you proposing or supporting in this area?

Dr. Lindberg: The Long Range Planning Panel for Toxicology and the Environment met three times in the November 1991 - March

1992 period. At this time, the various recommendations made by the Panel are being integrated into a draft report that will be circulated several times through the Panel before being completed. The final report then will be submitted to the Library's Board of Regents.

It is too early to list the new activities, stemming from Panel recommendations, for which the Library will seek support. However, at this preliminary stage, the following proposed projects and activities seemed of particular interest:

Strengthening traditional library services for the toxicology and environmental health areas.

Improved internal integration of the existing NLM online databases in toxicology through the use of modern information technologies.

Providing better access for users to toxicology and environmental health information in NLM databases or in other databases that are located in other governmental or private sector information systems, in this country as well as abroad.

Exploration of the use of modern information technologies to assist molecular biology researchers in linking toxic events to activities by chemicals or other agents on biological systems such as DNA or proteins.

Enhancing NLM information services to be maximally useful for chemical emergency response activities.

Improving NLM's interactions with international database activities in toxicology and environmental health.

Mr. Stokes: Are you in the process of establishing a mechanism which would strengthen the capacity of HBCU's to train medical and other health professionals in the use of information resources in this area? To what extent would you support the establishment of such a mechanism? What level?

Dr. Lindberg: The National Library of Medicine is in the process of establishing a mechanism which would strengthen the capacity of HBCUs to train medical and other health professionals in the use of our toxicological, environmental, and occupational information resources. This process began last summer with the selection of nine HBCUs whose graduates represent the majority of the health professionals that practice or work in the underserved communities of color in this country. These HBCU institutions are:

Drew University School of Medicine and Science
Florida A & M University
Howard University
Meharry Medical College
Morehouse School of Medicine

Texas Southern University
Tuskegee University
University of Arkansas, Pine Bluff
Xavier University

Representatives from each of these institutions have been provided extensive training in the use of NLM's databases; materials and support to conduct training classes at their home institutions; PC-based workstations; and free access to the Library's on-line files for an experimental period of one year. For the remainder of this one-year period, we will continue to provide assistance to the institutions involved in this project in order to increase the level of awareness and optimize the use of our resources in addressing health care information needs within the HBCU communities.

Within the near future, we will look into extending this outreach effort to other minority schools with programs in the environmental, occupational or hazardous wastes areas. This extension will be in collaboration with the Agency for Toxic Substances and Disease Registry (ATSDR) wherein ATSDR would support the training of personnel from at least ten other HBCUs and NLM would provide free searching of our databases by these institutions for a limited period.

Minority Efforts

Mr. Stokes: How many and what percentage of employees of your institute are minorities? Please provide a breakdown by race and grade level. How many are employed in a research capacity?

Dr. Lindberg: The statistics are as follows:

Grade Level	Black	Hispanic	American Indian	Asian/ Pacific Is.
GS-04	11			1
GS-05	8	2		4
GS-06	15	3		5
GS-07	28	1		1
GS-08	11			
GS-09	9		1	2
GS-10	1			
GS-11	10	1		5
GS-12	13	2		14
GS-13	4			2
GM-13	2			1
GM-14	2			
GM-15	2			1
SES	1			
Special Expert	1			
Staff Fellow				1
Visiting Scientist				1
Total	118	9	1	38

Of a total of 549 employees, 30 percent are minorities.

There are 18 minorities employed in NLM's research organizations; the National Center for Biotechnology Information and the Lister Hill Center for Biomedical Communications.

Mr. Stokes: Please describe for the Committee the resources and funding levels which will be provided for minority-specific research activities in FY 1993? How do these levels compare to last year's levels? Total funding represents what percentage of your budget?

Dr. Lindberg: The NLM supports several specific minority activities. These activities include:

The Information Access Project at Meharry Medical College. Over 300 faculty, residents, students, and practicing health professionals have been trained to use Grateful Med and MEDLINE. Off campus, workstations have been established in the offices of eight health professionals (Meharry preceptors) practicing in rural and inner city locations in Tennessee; these will be expanded to 23 by 1993.

An Undergraduate Research Study Program to stimulate undergraduate medical informatics research programs in Historically Black Colleges and Universities (HBCUs) for electrical engineering and computer science students. Four electrical engineering students from three institutions--Morgan State University, Southern University at Baton Rouge, and North Carolina A & T State University--comprise the first class. These students will complete two school year R&D assignments and two summer internships at the Lister Hill Center.

A new initiative in the Toxicology Information Program to establish mechanisms to strengthen the capacity of nine Historically Black Colleges and Universities (HBCUs) to train medical and other health professionals in the use of toxicological, environmental, occupational, and hazardous waste databases at NLM. Pilot strategies are being developed to utilize these HBCUs as vital information channels to reach minority and underserved populations who are disproportionately exposed to hazardous materials at home and in the workplace. In 1993, training in the use of NLM databases will be extended to persons living in the communities served by these HBCUs.

Projects through the National Network of Libraries of Medicine (NN/LM) to identify health professionals in underserved areas and encourage them to gain access to information through electronic sources such as Grateful Med. Thirty-three of these projects are directed at health professionals serving minority populations.

The spending level for these minority programs is:

1992	$726,000	0.7% of total budget
1993	$753,000	0.7% of total budget

NLM is researching a new outreach initiative in the Lower Mississippi Delta. The purpose is to improve access to health information, with the ultimate goal of improving the quality of health care delivery in this 214 county, seven state region characterized as the most impoverished area of the nation.

Mr. Stokes: To what extent are you working with the Office of Minority Health to effectuate these goals?

Dr. Lindberg: The OMH is apprised of all NLM minority activities. NLM is also involved with NICHD and OMH on their Minority Health Behavior Initiatives; we have pledged NLM's resources and support.

General Lack of Access

Mr. Stokes: In your statement prepared for today, you note that "It is unfortunately true that many American health professionals do not have easy access to computerized biomedical information..." What type of factors contribute to this lack of access?

Dr. Lindberg: Factors contributing to health professionals' lack of access to computerized biomedical information include: geographic isolation in rural or inner city areas without good library facilities; lack of affiliation with a hospital or medical school library that provides information services and training in the use of new information products; lack of knowledge of the information services that can be available to them irrespective of their location; and lack of appreciation of how available information services can improve their health care decisions.

Mr. Stokes: How is the Library addressing this issue? What are your specific goals in this area?

Dr. Lindberg: The National Library of Medicine is attempting to increase access to information services by American health professionals by: (1) developing and improving products like Grateful Med® and Loansome Doc® that can provide low-cost information to health professionals irrespective of their geographic location or lack of current affiliation with a hospital or medical library; (2) connecting unaffiliated health professionals with the services of the National Network of Libraries of Medicine (NN/LM); (3) publicizing available information products and services through contact at professional meetings, demonstrations, exhibits, training sessions, articles in professional journals, etc.; (4) designing specific outreach projects to reach health professionals working in rural areas and/or serving minority populations; and (5) highlighting the results of studies and other evidence that access to current information can have a significant positive effect on the outcome of patient care. To date, NLM has funded outreach projects in 48 states. The eventual goal of NLM's Outreach program is to make NLM and NN/LM services both known and readily accessible to all U.S.

health professionals. Specific objectives for the next year include: (1) analysis of the results of the first 30 individual library outreach projects to identify successful strategies; (2) development of a Mississippi Delta outreach to other disadvantaged regions that encompass parts of several states; (3) initiation of a number of additional small outreach projects in rural and inner city areas.

Mr. Stokes: To what extent are you working with the Regional Medical Libraries?

Dr. Lindberg: The Regional Libraries and the entire NN/LM network is an integral part of NLM's outreach efforts. In FY 1991, the network was reconfigured from seven to eight Regions in order to improve the ability of the Regional Medical Libraries to direct outreach efforts in the Northeastern United States, which includes the largest number of health professionals of any region in the country and encompasses both major inner city areas and remote rural areas. The new RML contracts include specific staffing and program responsibility for outreach. A major part of the responsibility for making direct contact with individual health professionals, exhibiting and demonstrating NLM's products and services at state, Regional and National meetings, and providing training to health professionals is borne by the RMLs. The RMLs also assist other network libraries in carrying out their individual outreach projects and identifying and developing larger outreach projects within their Regions.

Outreach

Mr. Stokes: The Committee understands that the National Library of Medicine is developing a new outreach initiative in the Lower Mississippi Delta, one of the most underserved regions of the nation in terms of providing health care for its people. What are the overall goals of NLM's Lower Mississippi Delta Project?

Dr. Lindberg: Portions of some seven states directly attached to the Mississippi River from the Gulf of Mexico South to Southern Illinois North have been characterized as the most impoverished region in the nation. Some 214 counties in these seven states are classified well below the poverty level. The region involves some 8.3 million people. The history of the region has been one of depression, inadequate education, poor economic development and extremely high unemployment. It is an area in which health care is extremely inadequate. Infant mortality per 1,000 people in the Delta is 20% greater than the rest of the nation. Compared to the European Americans, the rate for African Americans in the region is more than double. Statistics compiled since 1969 show that the percent change has not decreased or the gap has not narrowed. For some counties in Mississippi, Missouri, Arkansas and Louisiana, infant mortality rates are greater than for several third world countries such as Chile, Malaysia and Cuba, but again for the African American Delta population the rate is two to three times greater.

There are far fewer health care professionals practicing in the Delta region than in the non-Delta parts of the United States. This inequity is particularly pronounced when comparing rural areas. Although the number of physicians serving the urban Delta is about the same as those serving other urban areas, there are 90% fewer physicians serving the rural Delta than other rural areas of the Nation.

The shortage of registered nurses practicing in the area is even worse than that of physicians. The number of nurses in the rural Delta region is only about one-fourth of the average for rural nurses nationally. The number of urban Delta nurses is about two-thirds of the average in other urban areas. Few if any other allied health professionals are located in the rural parts of the region. Several health care professionals and clinics are moving out of the region making it even more difficult for people in the area to have access to health care.

As the major resource for health information in the nation, the National Library of Medicine in conjunction with the National Networks of Libraries of Medicine (NN/LM) seeks to initiate a major outreach initiative in the Lower Mississippi Delta for the purpose of improving access to health information, with the ultimate goal of improving the quality of health care delivery in the region. The project should create awareness of NLM information products and services; promote their use in health care situations by practicing health professionals in the region; and provide NLM with information about the effectiveness of the outreach strategies and the usefulness of the information resources as means for improving the practice behaviors of health professionals and the health outcomes of their patients.

Mr. Stokes: How will the proposed planning conference help NLM to achieve its objectives of improving access to the Library's information resources by health professionals practicing in the region?

Dr. Lindberg: NLM's initial effort includes organizing a local conference in which we will assemble major health professionals, political and other interested persons to help identify and plan NLM's role. This conference is intended to define suitable mechanisms and outreach strategies that NLM may employ in collaboration with the region's health leaders and community based institutions, by:

Providing participating health leaders and representatives of community-based institutions with an understanding of NLM, its information technologies, and its overall outreach objectives.

Defining the Lower Mississippi Delta's health care problems and constraints that may benefit from improved access to national information resources and identify the information needs of health professionals practicing in the Lower Mississippi Delta region.

Determining critical focal points in different geographic areas and/or states in the region, including the names of specific individuals and institutions who may serve as likely collaborators with NLM.

Identifying and discussing potential collaborative outreach projects -- in the form of new strategies and mechanisms -- that are intended to:

(1) create awareness of NLM and the National Network of Libraries of Medicine information products and services;
(2) promote their use in health care situations by practicing health professionals in the region; and
(3) evaluate both the effectiveness of the outreach strategies and the usefulness of the information resources as means for improving the practice behaviors of health professionals and the health outcomes of their patients.

Enabling NLM staff to finalize plans for a comprehensive Lower Mississippi Delta Outreach Program, including the specification of near- and long-term budgetary requirements.

Mr. Stokes: In your professional judgment, what resources will be required to implement this project?

Dr. Lindberg: Our professional judgment is that at least $2 million will be required to implement this project.

Manpower Needs and Training

Mr. Early: Doctor, would you give us a brief overview of research training needs as they pertain to your Institute?

Dr. Lindberg: There is a growing need for qualified talented investigators prepared to address information problems in health care, health professions education, and biomedical research. In addition to the documented need for researchers in medical informatics (knowledge representation, decision-making, expert systems, artificial intelligence, etc.), now more specialized needs are being identified, such as high performance computing and communicative biotechnology informatics, radiation therapy, radiologic diagnosis, and hospital information systems.

Mr. Early: How does your budget request address these needs?

Dr. Lindberg: The current budget is barely able to accommodate basic training needs in medical informatics. Needs of the more specialized areas are met less well.

Mr. Early: Could more resources be spent effectively?

Dr. Lindberg: More resources would permit more students to enter the funded programs and permit some specialized tracks in areas such as biotechnology, HPCC, and radiation treatment.

Outreach and Education

Mr. Early: What is the status of your efforts to implement the recommendations of the DeBakey outreach panel?

Dr. Lindberg: The recent report of the NLM Board of Regents on Improving Health Professionals' Access to Information, published as an update to the NLM Long Range Plan, and based on the work of a distinguished panel chaired by Dr. Michael DeBakey, recommends: (1) major enhancements to NLM's national network as a way of improving NLM's outreach to health professionals; (2) expanding health professionals' access to national information sources; (3) substantial increases in the number of Medical Informatics training centers, individual awards for research and career development and demonstration grants; and (4) research to ascertain the information requirements of U.S. health professionals, the suitability of current means for acquiring health-related information, and impediments to such acquisition, with an emphasis on the needs of minority health professionals and other underserved groups.

Outreach continues to be a high priority. NLM continues to invest both its fiscal and intellectual resources not only in acquiring scientific information but in devising new and more efficient and effective methods for making it readily available to the health and scientific community. We have reorganized the Regional Medical Library Network into a new outreach-oriented National Network of Libraries of Medicine (NN/LM), adding an eighth region serving New England; increased the number of Medical Informatics training centers from 7 in FY 91 to 10 in FY 92; completed a study of MEDLINE users employing the Critical Incident Technique which found that MEDLINE is an extremely valuable resource for patient care information, in addition to its use for research purposes and other professional activities; and initiated 120 outreach projects (up from 16 in 1989), including:

Extensive efforts to train physicians and other health professionals on the use of GRATEFUL MED in almost 50 communities, through special projects at the Regional Medical Libraries and awards to individual small-to-medium sized libraries in the network, with an emphasis on libraries in rural and inner city areas.

Through the Information Access Project at Meharry Medical College, over 300 faculty, residents, students, and practicing health professionals have been trained to use Grateful Med and MEDLINE. Off campus, workstations have been established in the offices of eight health professionals (Meharry preceptors) practicing in rural and inner city locations in Tennessee; these will be expanded to 23 by 1993. This project is giving us significant insights into impediments or barriers that prevent health professionals from accessing online information sources as part of their daily routine (i.e. lack of awareness of Grateful Med, lack of hardware and software, need for training in online searching, need for demonstration of cost-benefits of online searching, physical isolation from a library and sources of information). More than merely identifying the barriers, the project seeks to find ways to turn the barriers into opportunities for change.

A major outreach initiative is being planned for implementation in 1993 in the Lower Mississippi Delta to extend library services and access to clinically relevant computer databases among care givers practicing in this 214 county, seven state region characterized as the most impoverished area of the nation.

A pilot project is underway now in the Lower Mississippi Delta at the rural clinic of Dr. Anne Brooks, an individual practitioner serving a predominately minority population in Tutwiler, Mississippi. Dr. Brooks is providing NLM with valuable feedback on the usefulness of Grateful Med access for patient care in this setting.

In the Lower Rio Grande Valley of Texas, the benefits of MEDLINE searching have been demonstrated by an innovative outreach program that traveled a circuit-rider librarian to 10 hospitals and clinics that otherwise would have gone without access to current medical information.

An Undergraduate Research Study Program to stimulate undergraduate medical informatics research programs in Historically

Black Colleges and Universities (HBCUs) for electrical engineering and computer science students. Four electrical engineering students from three institutions--Morgan State University, Southern University at Baton Rouge, and North Carolina A & T State University--comprise the first class. These students will complete two school year R&D assignments and two summer internships at the Lister Hill Center. The program will be expanded in 1993 to provide modest support to the participating universities for equipment for the students.

A new initiative in the Toxicology Information Program is establishing mechanisms to strengthen the capacity of nine Historically Black Colleges and Universities (HBCUs) to train medical and other health professionals in the use of toxicological, environmental, occupational, and hazardous waste databases at NLM. Pilot strategies are being developed to utilize these HBCUs as vital information channels to reach minority and underserved populations who are disproportionately exposed to hazardous materials at home and in the workplace.

Mr. Early: What is NLM doing to get needed information into the hands of the doctors in the rural and isolated areas of the country?

Dr. Lindberg: It has become evident that large numbers of health professionals do not have easy access to biomedical information--because of geographic isolation, non-affiliation with a hospital or medical school library, or lack of information about NLM's products and services. With the increased funding available for outreach, we have identified institutions and individuals to help us reach out to these underserved health professionals; libraries in our own Regional Medical Library network have stepped forward, as well as other institutions, in response to NLM solicitations for help. These outreach initiatives include:

Projects through the National Network of Libraries of Medicine (NN/LM) to identify health professionals in underserved areas and encourage them to gain access to information through electronic sources such as Grateful Med. 33 projects have a minority focus.

Faster and easier access to documents identified in online searches. For those health professionals who are not affiliated with a medical library, LOANSOME DOC, NLM's new link between the GRATEFUL MED user and a network library, allows electronic ordering of documents.

Demonstration projects in the Rio Grande Valley of South Texas and Meharry Medical College in Tennessee to identify impediments to use and test innovative strategies for improving access among health professionals serving predominantly minority populations in geographically isolated areas, including the use of a circuit librarian (Rio Grande Valley) and training residents in GRATEFUL MED use, who will go on to train their preceptors (Meharry).

Continuing efforts to publicize the programs and services of the Library. Publicity activities are targeted both to health professionals and to general audiences, and include exhibits at meetings as well as training kits, press releases, videos, and a campaign to inform dental professionals about the benefits of GRATEFUL MED.

NLM's initiatives in high performance computing and networking go hand in hand with its outreach programs. High speed computer networks will be the avenue of choice for the dissemination of much biomedical information in coming years. It is not enough to publicize NLM's products and services without assisting institutions in connecting to national information resources, nor is it enough to provide high-technology innovations without reaching out to ensure that everyone has access to the new technology. A number of steps are being undertaken to assure the participation of HBCUs and health professionals in under- and unserved areas. Through the HPCC initiative, funds will be available to academic health science libraries, and to smaller hospital libraries, to provide connections to the national high speed network. The purpose of these efforts is to facilitate access to and delivery of health sciences information via pathways employing the most up-to-date and effective computer and telecommunications technology available.

Mr. Early: In your professional judgment, what resources are needed to effectively enhance NLM's outreach program?

Dr. Lindberg: My professional judgment budget included $48.0 million for this purpose in FY 1993. Funding of outreach activities would eventually be in accordance with the amounts recommended by the recent DeBakey Outreach Planning Panel to increase the Library's effort to improve access to its information services by every American professional in all settings. In order to accomplish this, NLM must restructure the Regional Medical Library (RML) network and enhance the RML contracts with greatly expanded outreach responsibilities, increase the number of Resource Access Grants and bring the Integrated Academic Information Management Systems (IAIMS) program closer to its originally envisioned level of support; increase the number of training grants and fellowships; expand evaluation, publicity and promotion efforts; and develop a production line of new products and services.

Preservation

Mr. Early: What is the current target date for completion of the preservation project?

Dr. Lindberg: Preservation of the NLM collection is an ongoing responsibility. Although the program as a whole must continue indefinitely, the current target date for completion of microfilming or copying to another permanent medium the Library's endangered brittle books and journals is 2011. By the end of 1992, NLM will have microfilmed about 34% of the estimated 60 million brittle pages in its book and journal collection. The amount of new biomedical literature printed on acidic paper is diminishing rapidly, due in part to NLM's successful campaign to persuade publishers to use more permanent paper in new publications. Between the volumes in the NLM collection that are already brittle and are therefore part of the current microfilming program and the newly published works published on permanent, alkaline paper, however, are hundreds of thousand of NLM volumes that are printed on acidic paper that is not yet brittle. Deacidification will probably be an option for this material. While this treatment is much less expensive than copying the content of volumes to another medium, NLM will still require preservation resources after 2011 to obtain deacidification services, to continue routine binding of new acquisitions and conservation of the rare and unique materials in it collection, and to address the preservation of theses, pamphlets, audiovisual programs, and machine-readable data.

Mr. Early: How much is included in your FY 1993 request for preservation efforts and will this amount enable NLM to stay on schedule for completion of this project?

Dr. Lindberg: NLM's FY 1993 budget request includes $2,168,000 for all aspects of preservation including staffing, microfilming, binding, conservation of rare and unique materials, and collection storage and maintenance. At this rate, the time required to complete microfilming or otherwise copying the contents of the brittle volumes currently in the NLM collections will be completed by 2011, our present schedule.

Budget Needs

Mr. Early: What was the NLM's original budget request and how does it differ from the request before us?

Dr. Lindberg: NLM's FY 1993 budget request to NIH was $216,678,000. The request to NIH included funds as follows:

- Outreach

  The Outreach effort would be supported at the level recommended by the DeBakey report, including enhancing the Regional Medical Library contracts with expanded outreach responsibilities, providing additional support for Resource Access Grants and Training Grants, augmenting evaluation, publicity and promotion efforts, and expanding development of new projects and services.

- High Performance Computing and Communications (HPCC)

  The HPCC Program would be supported at the level recommended by the FCCSET (Federal Coordinating Council on Science, Engineering, and Technology) Committee on Physical, Mathematical, and Engineering Sciences for expanding networking efforts to foster the use of communications and information processing technologies to link and relate library systems with individual and institutional databases and files for patient care, research, education, and administration within and between medical centers.

- Medical Informatics Research

  Grant-supported activities would be significantly expanded as related to the research resources directed to the logical aggregation of information, synthesis and analysis, and the development of knowledge systems that focus on more intelligent information processing.

- Preservation

  Deacidification of NLM's many acidic, but not yet brittle volumes, would be supported, along with initiating preservation of brittle pamphlets and theses in NLM's collection and expanding support for preservation of important materials held by other biomedical libraries, but not by NLM.

- Computer

  Due to the continuing growth in NLM's data processing requirements and to support NLM's linkage with national networks, the upgrade of NLM's current computer system to a system with greater capacity would be supported.

- Biotechnology

  The National Center for Biotechnology Information and the extramural biotechnology grants would have sufficient funding for necessary staffing levels, an increased number of grants in bioinformatics, education and training of experimental scientists in computer methods, and adequate funding for the development of computer databases and software to support the rapidly growing field of molecular biology.

- Unified Medical Language System (UMLS)

  The development of the UMLS project and the testing and evaluation of the UMLS knowledge sources by expanded development contracts and increased grant support for investigator-initiated research involving the UMLS knowledge sources would be accelerated.

- Agency for Health Care Policy and Research

  Rapid progress would be made in improving NLM's coverage of health services research, providing special literature search service to an increasing number of groups generating practice guidelines, developing new databases and services to assist the generators and users of health services research, expanding the utility of the UMLS knowledge sources to analysis of patient record data, and supporting investigator-initiated research to develop enhanced information processing techniques for outcomes research involving automated patient data.

- AIDS

  A single point user-initiated online access system (Gateway) for facilitating access to AIDS and related medical information would be established so that agencies would not have to duplicate existing online databases nor maintain multiple and duplicative copies on differing computing systems.

Priorities

Mr. Early: If an increase were provided over the budget request, how would you use these additional funds?

Dr. Lindberg: NLM priorities are as follows:

- Basic Library Services

  With funds to maintain NLM's basic library services, NLM would be able to acquire the world's current output of scholarly biomedical literature and to make reasonable headway on preserving the information in deteriorating volumes, manuscripts and films already in the NLM collection. Work to expand and upgrade NLM's indexing of t the biomedical literature would be supported. In addition, NLM's current computer system would be upgraded to a system with greater capacity, due to the continuing growth in NLM's data processing requirements.

- Outreach

  As recommended by the recent DeBakey Outreach Planning Panel to increase the Library's efforts to improve access to its information services by every American health professional in all settings, NLM would restructure the Regional Medical Library (RML) network and enhance the RML contracts with greatly expanded outreach responsibilities; increase the number of Resource Access Grants and bring the Integrated Academic Information Management Systems (IAIMS) program closer to its originally envisioned level of support; increase the number of training grants and fellowships; expand evaluation, publicity and promotion efforts; and develop a production line of new products and services.

- High Performance Computing and Communications

  As recommended by the High Performance Computing and Communications Plan of the FCCSET (Federal Coordinating Council on Science, Engineering, and Technology) Committee on Physical, Mathematical, and Engineering Sciences, NLM would expand molecular biology computing, create and transmit libraries of electronic images, support the linking of academic health centers via computer networks, create "intelligent gateways" to retrieve information from multiple life sciences databases and expand training in biomedical computer science.

- Biotechnology

  The National Center for Biotechnology Information and the extramural biotechnology grants would have funding for increased staffing levels, an increased number of grants in bioinformatics, education and training of experimental scientists in computer methods, and funding for the development of computer databases and software to support the rapidly growing field of molecular biology.

- Medical Library Assistance

  Grant-supported activities would be significantly expanded as related to the Integrated Academic Information Management Systems (IAIMS) program and the Medical Library Resource Grants program, including the Information Access Grant and the Information Systems Grant.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

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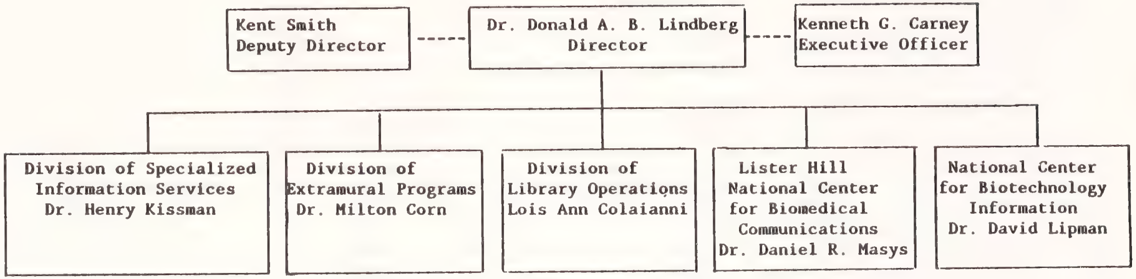
NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Organization Structure



NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

For carrying out section 301 and title IV of the Public Health Service Act with respect to the National Library of Medicine, [$100,303,000] $108,662,000: Provided, That of the funds made available under this heading, $3,500,000 shall not become available for obligation until September 30, [1992] 1993.

(Departments of Labor, Health and Human Services, and Education and related Agencies Appropriations Act, 1992.)

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Amounts Available for Obligation 1/

	1991 Actual	1992 Appropriation	1993 Estimate
Appropriation	$91,408,000	$100,303,000	$108,662,000
Sequester order	-1,000	---	---
Enacted administrative reduction	---	---	---
Section 214 reduction	---	-80,000	---
Section 513 reduction	---	-900,000	---
Subtotal, adjusted appropriation	91,407,000	99,323,000	108,662,000
Comparative transfer from:			
National Institute of General Medical Sciences for GENBANK	+3,400,000	+4,000,000	---
Subtotal, adjusted budget authority	94,807,000	103,323,000	108,662,000
Unobligated balance lapsing	-225,000	---	---
Total, Obligations	94,582,000	103,323,000	108,662,000

1/ Excludes the following amounts for reimbursable activities carried out under this account: 1991: $13,113,214; 1992: $15,607,000; 1993: $16,185,000.

NATIONAL INSTITUTES OF HEALTH
National Library of Medicine
Budget Mechanism

(Dollars in Thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	No.	Amount	No.	Amount	No.	Amount
Extramural Programs:						
Grants:						
Noncompeting	64	$16,071	54	$11,927	66	$16,532
Competing	48	3,920	44	8,632	35	4,944
Subtotal, Grants	112	19,991	98	20,559	101	21,476
Contracts:						
Noncompeting	--	---	8	5,500	8	5,704
Competing	8	5,500	--	---	--	---
Subtotal, Contracts	8	5,500	8	5,500	8	5,704
Total, Extramural	120	25,491	106	26,059	109	27,180
	FTEs		FTEs		FTEs	
Intramural Programs:						
Library Operations	338	36,180	351	38,427	351	40,481
Lister Hill Center	82	11,774	80	14,976	80	16,316
Biotechnology Center	27	9,177	34	10,514	34	10,767
Toxicology Information	40	4,742	40	5,170	40	5,387
Total, Intramural	487	61,873	505	69,087	505	72,951
Research Management and Support	98	7,443	108	8,177	108	8,531
Total Budget Authority	585	94,807	613	103,323	613	108,662

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

CROSSWALK - 1991 ACTUAL

Program Activity	Mechanism Extramural Programs Grants	 Contracts	 Intramural Programs	 Research Mgmt. and Support	 Total
Extramural Programs					
Medical Library Assistance....	$9,191	$5,500	---	---	$14,691
Medical Informatics...........	10,800	---	---	---	10,800
Total, Extramural...........	19,991	5,500	---	---	25,491
Intramural Programs					
Library Operations............	---	---	36,180	---	36,180
Lister Hill Center............	---	---	11,774	---	11,774
Biotechnology Center..........	---	---	9,177	---	9,177
Toxicology Information..........	---	---	4,742	---	4,742
Total, Intramural...........	---	---	61,873	---	61,873
Research Management and Support.	---	---	---	7,443	7,443
Total Budget Authority......	19,991	5,500	61,873	7,443	94,807

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

CROSSWALK - 1992 Appropriation

Program Activity	Mechanism				
	Extramural Programs				
	Grants	Contracts	Intramural Programs	Research Mgmt. and Support	Total
Extramural Programs					
Medical Library Assistance....	$9,191	$5,500	---	---	$14,691
Medical Informatics..........	11,368	---	---	---	11,368
Total, Extramural..........	20,559	5,500	---	---	26,059
Intramural Programs					
Library Operations...........	---	---	38,427	---	38,427
Lister Hill Center...........	---	---	14,976	---	14,976
Biotechnology Center.........	---	---	10,514	---	10,514
Toxicology Information.........	---	---	5,170	---	5,170
Total, Intramural..........	---	---	69,087	---	69,087
Research Management and Support.	---	---	---	8,177	8,177
Total Budget Authority......	20,559	5,500	69,087	8,177	103,323

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

CROSSWALK - 1993 Estimate

	Mechanism				
	Extramural Programs				
Program Activity	Grants	Contracts	Intramural Programs	Research Mgmt. and Support	Total
Extramural Programs					
Medical Library Assistance....	$9,531	$5,704	---	---	$15,235
Medical Informatics..........	11,945	---	---	---	11,945
Total, Extramural..........	21,476	5,704	---	---	27,180
Intramural Programs					
Library Operations............	---	---	40,481	---	40,481
Lister Hill Center...........	---	---	16,316	---	16,316
Biotechnology Center..........	---	---	10,767	---	10,767
Toxicology Information..........	---	---	5,387	---	5,387
Total, Intramural..........	---	---	72,951	---	72,951
Research Management and Support.	---	---	---	8,531	8,531
Total Budget Authority......	21,476	5,704	72,951	8,531	108,662

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Summary of Changes

1992 Estimated budget authority	$103,323,000
1993 Estimated budget authority	108,662,000
Net Change	+5,339,000

	1992 Current Estimate Base		Change from Base	
	Pos. (FTEs)	Budget Authority	Pos. (FTEs)	Budget Authority
Changes:				
A. Built-in:				
1. FY 1993 pay raise		$31,647,000		+1,030,000
2. Within-grade increase		31,647,000		+308,000
3. Annualization of January 1992 pay raise		31,647,000		+357,000
4. One less day of pay		31,647,000		-122,000
5. Service and supply fund increase		1,339,000		+50,000
6. Payment for centrally furnished services		8,455,000		+151,000
7. Increased cost of supplies, materials, literature and other expenses		41,380,000		+1,692,000
8. DHHS Working Capital Fund		188,000		+9,000
Subtotal				+3,475,000
B. Program:	No.	Amount	No.	Amount
1. Grants:				
a. Noncompeting	54	11,927,000	+12	+4,605,000
b. Competing	44	8,632,000	-9	-3,688,000
Total	98	20,559,000	+3	+917,000
2. Contracts:				
a. Noncompeting	8	5,500,000	---	+204,000
b. Competing	---	---	---	---
	FTEs		FTEs	
3. Intramural Programs	---	69,087,000	---	+743,000
4. Research Management & Support	---	8,177,000	---	---
Subtotal				+1,864,000
Total changes				+5,339,000

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Budget Authority by Activity

(Dollars in Thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	No.	Amount	No.	Amount	No.	Amount
Extramural Programs						
Med'l. Library Assistance.....		$14,680		$14,691		$15,235
Medical Informatics...........		10,800		11,368		11,945
Total, Extramural...........		25,480		26,059		27,180
Intramural Programs						
Library Operations.............	338	36,131	351	38,427	351	40,481
Lister Hill Center.............	82	11,735	80	14,976	80	16,316
Biotechnology Center...........	27	9,094	34	10,514	34	10,767
Toxicology Information.........	40	4,699	40	5,170	40	5,387
Total, Intramural........	487	61,659	505	69,087	505	72,951
Research Management and Support.........................	98	7,443	108	8,177	108	8,531
Total, Obligations..............	585	94,582	613	103,323	613	108,662
Unobligated Balance Lapsing......		225				
Total, Budget Authority..........	585	94,807	613	103,323	613	108,662

National Library of Medicine

Budget Authority by Object

	1992 Appropriation	1993 Estimate	Increase or Decrease
Total number of full-time permanent positions................	527	527	---
Total compensable workyears:			
Full-time equivalent employment.....	633	633	---
Full-time equivalent of overtime and holiday hours.................	8	8	---
Average ES salary.....................	$103,666	$106,548	+2,882
Average GM/GS grade..................	12.0	12.0	---
Average GM/GS salary.................	38,468	39,543	+1,075
Average salary, grades est. by act of July 1, 1944 (42 U.S.C. 207).....	54,255	55,767	+1,512
Average salary of ungraded positions...........................	18,013	18,519	+506
Personnel compensation:			
Permanent positions................	22,246,000	23,275,000	+1,029,000
Positions other than permanent......	3,413,000	3,550,000	+137,000
Other personnel compensation........	949,000	987,000	+38,000
Special personal services payments..	1,000	1,000	---
Subtotal, personnel compensation..	26,609,000	27,813,000	+1,204,000
Personnel benefits...................	5,013,000	5,214,000	+201,000
Benefits for former personnel.........	25,000	26,000	+1,000
Travel and transportation of persons..	370,000	408,000	+38,000
Transportation of things.............	91,000	94,000	+3,000
Rent, communications and utilities....	1,524,000	1,580,000	+56,000
Printing and reproduction............	1,332,000	1,381,000	+49,000

	1992 Appropriation	1993 Estimate	Increase or Decrease
Other services:			
Project contracts..................	$24,945,000	$26,529,000	+$1,584,000
Centrally furnished services........	8,455,000	8,717,000	+262,000
Other..............................	6,501,000	6,765,000	+264,000
Supplies and materials................	473,000	491,000	+18,000
Equipment.............................	2,659,000	2,758,000	+99,000
Literature............................	4,767,000	5,458,000	+691,000
Grants, subsidies & contributions.....	20,559,000	21,476,000	+917,000
Total budget authority by object	103,323,000	108,662,000	+5,339,000

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Significant Items in the Senate Appropriations Committee Report

Cost Recovery

The Senate in its report 102-104, page 143 stated "...Last year the Committee endorsed NLM's policy to create and maintain the MEDLARS data bases using appropriated funds and to recover full costs of access through user fees. The Committee supports the continuation of these operating policies both as a principle of cost-sharing and as a process for maintaining the integrity of the data bases."

Action Taken or to be Taken - The NLM is continuing its MEDLARS operating policies, using appropriated funds to create and maintain the databases and recovering full access costs through user fees.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1991 Amount Authorized	1992 Appropriation	1992 Amount Authorized	1993 Budget Request
Research and Investigation	Title III, Part A Section 301	42§241	Indefinite	$74,166,000	Indefinite	$78,597,000
National Library Medicine	Title IV, Part D Section 465-467	42§286	Indefinite		Indefinite	
Medical Library Assistance	Title IV, Part D Section 469-477	42§286b	Such sums as necessary	14,691,000	Such sums as necessary	15,235,000
Biotechnology Information	Title III, Part A Section 301 and	42§241	Such sums as necessary	14,466,000	Indefinite	14,830,000
	Title IV, Part D Section 478	42§286c	Such sums as necessary		Such sums as necessary	
Total Budget Authority				103,323,000		108,662,000

National Library of Medicine

Appropriation History

Year	Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1984	$49,616,000	$42,263,000	$41,963,000	$49,613,000
1985	51,320,000	43,820,000 3/	53,500,000 4/	55,910,000
1986	53,320,000	46,972,000 3/	60,000,000	57,808,000
1986 Sequester				-2,486,000
1987	56,408,000	61,588,000	62,088,000	61,838,000
1988	64,399,000	71,465,000	70,399,000	67,910,000
1989	70,626,000	64,836,000 3/	70,626,000	73,731,000
1990	78,729,000	83,311,000	80,729,000	82,932,000 5/
1990 Sequester				-1,071,000
1991	89,916,000	80,725,000	94,416,000	91,408,000
1991 Sequester				-1,000
1992	100,554,000	99,565,000	100,549,000	99,323,000 6/
1993	108,662,000			

1/ Reflects enacted supplementals, recissions and reappropriations.
2/ Reflects the September amendment; the original request was $47,677,000.
3/ Excludes funds for Medical Library Assistance Act programs not considered.
4/ Includes $7,500,000 for Medical Library Assistance Act programs under the Continuing Resolution. Does not include $607,000 transfer of unobligated balances from the Health Resources and Services Administration.
5/ Excludes enacted administrative reduction of $379,000.
6/ Excludes enacted administrative reduction of $980,000.

Justification

National Library of Medicine

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
585	$94,807,000	613	$103,323,000	613	$108,662,000	---	$5,339,000

General Statement

If Americans are to reap the maximum benefit from our investment in medical research, it is critical that physicians, scientists, educators, and other health care professionals have rapid and convenient access to the information generated. As the Nation's focal point for disseminating biomedical and developing and applying biomedical information technology, the National Library of Medicine (NLM) collects, organizes, and provides easy access to the world's published health knowledge. Programs under way today will ensure that information continues to be available when and where it is required and in a form that can be readily used. NLM's ongoing outreach efforts to increase the availability of information, coupled with its role in the High Performance Computing and Communications (HPCC) program initiated by the President's Office of Science and Technology, increase and improve today's information access and hold promise of great future improvements.

Outreach continues to be NLM's highest priority. Because the demand for information by health professionals continues to grow, NLM is investing both its fiscal and intellectual resources not only in acquiring scientific information but in devising new and more efficient and effective methods for making it readily available. The Library is making special efforts to reach the many health professionals who do not have easy access to biomedical information because of geographic isolation, nonaffiliation with a medical library, or lack of information about available services. There is a specific emphasis on reaching the health professionals serving minority populations. Focusing on rural and inner city areas, NLM is making extensive efforts through the member institutions of the National Network of Libraries of Medicine to train physicians and other health professionals in the use of GRATEFUL MED. By utilizing GRATEFUL MED, those isolated and underserved health practitioners will have access to the immense NLM databases equal to that of their colleagues in more urban settings (who did 5 million computerized searches in 1991).

NLM's initiatives in High Performance Computing and Communications go hand in hand with its outreach programs. High speed computer networks will be the avenue of choice for the dissemination of much biomedical information in the coming years. It is not enough to publicize NLM's products and services without assisting institutions in connecting to national information resources, nor is it enough to provide high-technology innovations without reaching out to ensure that everyone has access to the new technology. NLM's HPCC program includes intramural and extramural research and development in several areas: molecular biology computing, creation and transmission of electronic images, the linking of academic health centers via computer networks, the creation of "intelligent gateways" to retrieve information from multiple databases, and training in biomedical computer science and medical informatics. Ongoing projects include the continued development of the "Visible Human" digital image library project and the Unified Medical Language System.

Purpose and Method of Operation

To maintain its information services in support of research, health care delivery, and education, the Library's programs are conducted and supported through the following budget activities: (1) extramural programs, (2) intramural programs, and (3) research management and support. The primary goal of these activities is to ensure maximum application of biomedical knowledge and state-of-the-art health care improvements resulting from advances in biomedical research.

Funding for the National Library of Medicine during the last 5 years has been as follows:

	Amount	FTE
FY 1988	$67,910,000	510
FY 1989	73,731,000	511
FY 1990	85,728,000	550
FY 1991	94,807,000	585
FY 1992	103,323,000	613

Overall Budget Policy

The FY 1993 budget request for the National Library of Medicine is $108,662,000, an increase of $5,339,000 over the comparable FY 1992 level of $103,323,000. The request includes support for 613 full-time equivalent (FTEs). The request continues to emphasize support for library operations including literature acquisition, management, dissemination, and preservation, and for grants in Integrated Academic Information Management Systems (IAIMS), training, medical informatics, biotechnology and other high priority research and development initiatives. The request includes continued funding for outreach efforts initiated in FY 1992. The request also includes funding for the High Performance Computing and Communications initiative. Overall, NLM programs will be maintained at approximately the current level.

The request includes $6,711,000 for Outreach activities; an increase of $239,000 from the FY 1992 estimate of $6,472,000. At this level NLM will continue its recent efforts to expand its outreach activities. The NLM will enhance the National Network of Libraries of Medicine, increase "Access" grants and contracts to hospitals, strengthen research training and fellowships, and promote awareness of the products and services of the Library.

The request also includes $18.8 million for High Performance Computing and Communications activities. At this level, NLM will (1) award grants and contracts to connect medical institutions to the high-speed network and to train scientists in the use of new computer capabilities, and (2) fund several vital projects related to high performance computing and communications such as the "Visible Human" project, the Unified Medical Language project, and the GenInfo database project.

For extramural programs, the FY 1993 request is $27,180,000, a $1,121,000 increase over the FY 1992 comparable level. The request will support a total of 109 awards. For biotechnology information activities, this request includes support for 16 grants, as compared to 18 in FY 1992. For IAIMS, this includes funding for two Phase II and four Phase-III noncompeting awards. One Phase-II competing award will also be made.

With regard to intramural programs, and research management and support activities, $3,864,000 and $354,000 increases are provided respectively. These increases will provide for services provided centrally, other built-in increases for personnel and basic operating program requirements, including $515,000 for literature acquisition costs. Also included is $4,000,000 for the transfer of the GenBank funding from the National Institute of General Medical Sciences (NIGMS).

Funding for the National Center for Biotechnology Information is $10,767,000 at the FY 1993 request level, compared to $10,514,000 in FY 1992, a $253,000 increase. This includes $4,000,000 for the GenBank funding. The remaining resources will support the continuation of projects that are key to the development of improved and enhanced biotechnology information services.

Management Improvements

As a service organization, the NLM is continually reviewing and improving its methods of accomplishing its mission. Productivity measurements are an integral part of the Library's day-to-day operation to ensure the timeliness and quality of NLM's response to the thousands of document delivery requests from remote users throughout the country and abroad. The Library's unique long range planning initiative continues to result in projects that improve access of researchers and health care providers to accurate, up-to-date information. Recent notable improvements include reconfiguration of the National Network of Libraries of Medicine, increased emphasis in publicizing NLM products and services, and enhancements to network capabilities.

National Library of Medicine

Extramural Programs

Authorizing Legislation - Sections 301, 465-467, and 469-477 of the Public Health Service Act. 1993 Authorization: Indefinite

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$25,491,000	$26,059,000	$27,180,000	+$1,121,000

The NLM's Extramural Programs Division provides a range of grants for research and development activities relating to the management, dissemination, and use of medical knowledge. Authorized by Public Health Service laws including the Medical Library Assistance Act (MLAA), these grants seek improved biomedical communication and knowledge access essential to the Nation in exploiting findings of health research in the advancement of medical education, practice and research. These grant activities represent the only Federal programs focusing on information issues that concern the entire health community.

Funding for the Extramural Programs during the last 5 years has been as follows:

FY 1988	$14,724,000
FY 1989	16,833,000
FY 1990	23,618,000
FY 1991	25,491,000
FY 1992	26,059,000

Rationale for Budget Request

The FY 1993 budget request for NLM's Extramural Programs is $27,180,000 which will support approximately 109 awards. This represents an increase of $1,121,000 over the FY 1992 estimate.

Medical Library Assistance

Integrated Academic Information Management System (IAIMS) Program

The IAIMS initiative is designed to create model computerized information systems to serve health professionals in complex academic health centers. Instead of the current situation in which each institution has a host of separate databases, which may not be accessible to administrator and health care giver alike, IAIMS fosters integration such that from a desk top terminal, the user can gain rapid access to various files and systems: e.g., patient records, laboratory tests and results, previous treatment protocols, pertinent bibliographic databases, remote files (such as a tumor registry in another state), administrative data, and clinical decision-making systems.

NLM provides support to assist in the planning, development, and implementation of IAIMS. There are now five institutions which have successfully competed for the third and final implementation phase of this program.

Medical Library Resource Grants

Resource Grants assist public and private, nonprofit health science libraries to establish, expand and improve library resources and information services to health personnel engaged in education, research and patient care. This program, which was recently restructured to emphasize the utilization of computer and telecommunications technologies, offers two types of grants: Information Access Grants and Information Systems Grants.

The Information Access Grant is directed towards the libraries of small and medium-size hospitals and similar health-related institutions and promotes access to information resources via new technologies. The Information Systems Grant, which also emphasizes computer and telecommunications technologies, is directed towards larger hospitals and academic health centers and encourages networking, connectivity and systems integration. For example, at the Alaska Health Sciences Library (AHSL), the state's largest health sciences library, a librarian will oversee the installation of computers in the state's hospitals and establish electronic linkages to the AHSL. The AHSL librarian will also train the hospital staffs to access the biomedical literature and the resources and staff of the AHSL.

Present emphasis for the resource grants is on facilitating connection to national databases by networks for both health professionals and librarians. As the new technology penetrates the workplace, biomedical information will more and more be seen as a vast national library, composed of a myriad of local collections which are available to all through computers and telecommunications.

Research Grants in Medical Librarianship and Medical Information Science

NLM offers assistance for research and career development opportunities in Health Science Librarianship and Information Science. Investigations in this program area include evaluation of managerial and organization structure for improved information service, studies of how health information professionals perceive their information requirements, and how medical institutions can utilize new technologies for higher levels of information access.

Research Training in Medical Informatics and Biotechnology Information

NLM is the prime supporter, nationally, of university programs which provide research training in medical informatics and the related subfield which deals with biotechnology and molecular biology. Such programs are designed to train investigators who are well-equipped to address fundamental issues in the management of health knowledge. Trainees in this program will contribute to the growth of information sciences by analyzing special structures for managing this knowledge, and by advancing the frontiers of computer science for organizing, retrieving, and utilizing health knowledge.

In FY 1991, seven institutional training grants were supporting about 70 individuals at the predoctoral or postdoctoral level. In addition, five individuals were being supported by individual postdoctoral fellowships. A review of the program indicates that a vast majority of the trainees are physicians and that they obtain academic appointments subsequent to their training. A highly competitive national recompetition for institutional training grants during FY 1991 resulted in awards being granted to ten institutions for training programs to begin in July, 1992. NLM will also continue its program of new investigator and research career development awards.

To fill a need for medical informatics professionals, NLM announced in late 1991 the creation of a new fellowship in applied informatics, which will provide up to two years of training for those interested in learning some aspect of informatics which can then be applied to their primary discipline. IAIMS, newer library methods, computerized patient records, informatics aspects of radiotherapy, dentistry, and nursing, artificial intelligence programs, and medical education are among the areas which may be studied by such fellows.

National Network of Libraries of Medicine (NN/LM)

The purpose of the National Network of Libraries of Medicine (formerly the Regional Medical Library Network) is to improve and equalize access to biomedical information in the United States by linking health professionals and researchers to the information resources they need, regardless of their geographic location. There are 3,600 network members including health sciences libraries of every size and type in all parts of the country. The NN/LM Program is a cornerstone of NLM's outreach program and its services are being revised and enhanced as part of NLM's expanded outreach initiative. In each multi-state region of the Network, NLM contracts with a distinguished medical library to coordinate network members within the Region to provide document delivery, encourage resource sharing, support use of online services, and develop innovative outreach services to health professionals. The Regional Medical Libraries (RMLs) are supported by more than 130 large Resource Libraries, generally in medical schools, and approximately 3,500 hospital and special libraries, individually and in consortia.

The network was reconfigured in FY 1991, from seven regions to eight. Results of network outreach initiatives include extensive efforts to train physicians and other health professionals in the use of GRATEFUL MED in almost 50 communities in 27 states. This is being accomplished through special projects at the Regional Medical Libraries, and awards to individual small-to-medium sized libraries in the network, with an emphasis on those in rural and inner city areas.

To assist the Regional Medical Libraries and other members of the network in carrying out their expanded responsibilities for exhibits, training sessions, and development of specific outreach projects, the NLM Network Office has developed training materials, special fact sheets, an exhibit management packet, and exhibit backdrops for use in all Regions, and conducted special training for RML employees who will exhibit NLM's products and services.

High Performance Computing and Communications

In consonance with this initiative, Extramural Programs plans to award grants to connect medical institutions to the high-speed network, to foster integrated information systems of which HPCC is an essential element, to support the informatics research necessary for full exploitation of the technological possibilities, and to train medical scientists and other health professionals in the use of new computer and telecommunication capabilities.

Outreach Initiative

NLM continues to build upon and enhance existing outreach activities to improve access by health professionals to NLM's information resources. The focus of these activities has been on enhancing the National Network of Libraries of Medicine (NN/LM) and on improving access by individual health professionals to NLM's information products and services, especially by persons presently unaffiliated with an institution and/or who are located in rural or other medically underserved settings.

Through the addition of special enhancements to the existing (NN/LM) contracts, the NLM has funded demonstration projects in twelve states to test varying means of increasing awareness of and access to NLM's information products and services. Another program, which was recently developed provides for small competitive contracts awarded directly by NLM to network libraries for the purpose of introducing online searching via GRATEFUL MED to health professionals in rural and inner city areas. All of these outreach efforts are aimed at linking underserved health professionals to the National Network; however, they should also encourage the NN/LMs and network member libraries to become more active partners with NLM in its outreach program.

In training, the newly established Fellowships in Applied Informatics have as one goal the training of professionals from underserved areas who can then return to their home institutions with the expertise needed to develop and implement modern biomedical information systems.

Medical Informatics

Medical Informatics Research

Through the medical informatics program, NLM supports work on fundamental knowledge issues. These concern the extraction, organization, retrieval, and utilization of knowledge, involving methodologies such as artificial intelligence-related computer sciences, computational linguistics, medical decision sciences, cognitive psychology, and related information-oriented fields.

Biotechnology Information Research

In the area of biotechnology information, extramural research is supported to investigate effective methodologies of reorganizing and analyzing data relating to molecular control of life processes. Relevant problems include designing and managing databases, retrieving information from multiple factual databases, and pattern-matching algorithms for biological sequences. Scientific advances in molecular biology will depend in large part on successful resolution of knowledge and information issues.

National Library of Medicine

Intramural Programs

Authorizing Legislation - Sections 301, 465-467, and 478 of the Public Health Service Act. 1993 Authorization: Indefinite

1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
487	$61,873,000	505	$69,087,000	505	$72,951,000	--	$3,864,000

NLM's intramural activities are carried out by four major components:

Library Operations - acquires and preserves library materials pertinent to medicine; organizes these materials by cataloging, indexing and bibliographical listing, publishes the catalogs, indexes and bibliographies; makes the literature available through bibliographic records in publications, online files, other machine-readable forms, loans, photographic or other copying procedures; and provides reference and research assistance. In addition, Library Operations assists in publicizing the availability of NLM products and services.

Lister Hill National Center for Biomedical Communications explores the use of computer, communication, and audiovisual technologies for the purpose of improving the organization, dissemination, and utilization of biomedical information.

National Center for Biotechnology Information - creates automated systems for knowledge about molecular biology biochemistry, and genetics; performs research into advanced methods on how to handle information about the vast number of biologically important molecules and compounds; enables those engaged in biotechnology research and medical care to use the systems and methods developed; and coordinates efforts to gather biotechnology information worldwide.

Toxicology Information Program (TIP) - develops computerized databases in the field of toxicology, pharmacology, and the environmental sciences and makes such information readily available to industry, academia, and Federal agencies. TIP is one of the Nation's most important sources of information for emergency response to toxic chemical spills and the release of health and environmental hazards.

Funding for the Intramural Programs during the last 5 years has been as follows:

	Amount	FTE
FY 1988	$46,762,000	419
FY 1989	50,304,000	424
FY 1990	55,022,000	454
FY 1991	61,873,000	487
FY 1992	69,087,000	505

Rational for the Budget Request

The FY 1993 budget request for Intramural Programs is $72,951,000. This is an increase of $3,864,000 above the FY 1992 appropriation which will provide for increased operation costs in FY 1993.

For FY 1993, the total amount requested for Intramural Programs includes $40,481,000 for Library Operations; $16,316,000 for the Lister Hill National Center for Biomedical Communications; $10,767,000 for the National Center for Biotechnology Information; and $5,387,000 for the Toxicology Information Program.

Library Operations

NLM's basic mission is to collect, organize, and provide access to the world's biomedical literature in support of the progress of medicine and the improvement of public health. In pursuit of this mission, the staff of Library Operations acquires and preserves the biomedical literature; organizes this literature through authoritative cataloging and indexing; disseminates authoritative NLM bibliographic records in publications, online files, and other machine-readable forms; lends or copies documents in the NLM collection as a back-up to document delivery service provided by other U.S. biomedical libraries; provides reference and research assistance to health professionals; and maintains an active program of scholarship in the history of medicine. Library Operations also directs the National Network of Libraries of Medicine or NN/LM (formerly called the Regional Medical Library Program) and cooperates with the Library of Congress and the National Agricultural Library to enhance the general level of library service available in the United States.

To improve the effectiveness and efficiency of NLM's unique biomedical information programs and services, Library Operations obtains assistance from commercial support contractors, makes regular and extensive use of advanced technology, and conducts research and evaluation projects related to its basic responsibilities.

Acquisition

The NLM collection now contains more than 4.9 million items including printed books, journal volumes, theses, pamphlets, audiovisuals, computer software, microforms, prints, photographs, and manuscripts. Library Operations staff select materials for the NLM collection, endeavoring to identify and acquire as soon as possible new and retrospective literature in all areas of biomedicine. In FY 1991, NLM added 43,105 volumes and 92,175 other items (e.g., audiovisuals, microforms, software, pictures, manuscripts) to its collection.

The Library conducts a complete review of its selection guidelines every 5 to 8 years. The Library has a program to assess how successful NLM has been in implementing its collection development policies and how well these policies serve the needs of health professionals and researchers. In FY 1991, the NLM staff reviewed NLM's collection of AIDS-related materials, recent dental monographs, and publications issued by associations and modified its acquisitions procedures to ensure better coverage of non-commercial publications. Several key improvements were made to the automated systems supporting acquisitions and processing.

Collection Preservation and Maintenance

The Library's preservation program includes: preserving and maintaining NLM's own collection, supporting the preservation of important biomedical literature not held by NLM, and promoting the use of more permanent materials in new biomedical publications. In FY 1991, NLM used contract assistance to microfilm about 2 million pages of brittle books and serial volumes.

FY 1991 was a transition year for the preservation program. A several year microfilming contract came to an end, and new competitive contracts were awarded for microfilming and for preservation and conservation of rare materials from NLM's historical collection. In FY 1991, NLM improved access to information about what it has microfilmed by updating CATLINE, its online catalog file, to indicate which books have been preserved. Information about serials NLM has preserved is already available in SERLINE. Microfilm service copies of items the Library has preserved are now available for purchase by other libraries and individual scholars. In an attempt to improve the quality of the binding service Federal libraries obtain, NLM took the lead role in revising the specifications for the Government Printing Office's library binding contract.

NLM's campaign to increase the use of acid-free paper in new biomedical publications has had very positive results. About 50% of the 3,024 Index Medicus titles are now known to be printed on acid-free paper. This represents a dramatic increase from 4% in 1987.

Creation of Bibliographic Data

NLM provides bibliographic control of the biomedical literature by: maintaining and enhancing the Medical Subject Headings (MeSH^R) and the NLM Classification; cataloging biomedical publications in all formats; and indexing articles from selected biomedical journals. In FY 1991, NLM cataloged 19,187 modern books, serials, non-print, and Cataloging-in-Publication galleys, using a combination of inhouse staff, contractors, and an interagency agreement with the Library of Congress. Because of a sharp increase in receipts, the inventory of uncataloged modern works increased by 4,359.

The Literature Selection Technical Review Committee, an NIH chartered committee, advises NLM on the journals that should be indexed and made accessible via MEDLINE. Based on their recommendations, NLM began indexing an additional 93 journals in 1991. About 363,000 indexed citations were added to MEDLINE during the year. NLM entered the author's abstract into the database for 72% percent of the articles. In its continuing effort to alert users to published data that have been identified as fraudulent, erroneous, or potentially flawed, the library added information to MEDLARS databases about 16 retractions, 2,722 published error notices, and 18,885 substantive commentaries on previously indexed articles.

Dissemination of Bibliographic Data

NLM disseminates its bibliographic data online, in various machine-readable formats, and in a series of publications ranging from Index Medicus, NLM's major index to about 3,000 biomedical journals, to Current Bibliographies in Medicine, which are relatively brief compilations of recent citations on specific topics of current interest. NLM's publications continue to be "best sellers" for the Government Printing Office and the National Technical Information Service.

NLM provides online access to 43 databases, including the MEDLINE and TOXLINE backfiles. In FY 1991, online users were connected to NLM's system for a total of 324,000 hours and conducted 5.8 million searches. These figures do not reflect use of MEDLARS data on the computer systems of other organizations that lease NLM files. As a result of outreach efforts by NLM and the National Network of Libraries of Medicine, the number of codes for use of NLM's online system continues its 6-year pattern of extremely rapid growth. At the end of FY 1991, there were 48,772 assigned codes, an increase of 23 percent from the end of the previous year. Most of the new codes were assigned to individuals rather than institutions. Individual users of NLM's online services now outnumber institutional users and represent 53 percent of all domestic code holders. Ninety percent of the individuals who received new codes in FY 1991 indicated an intention to use the Grateful Med^R microcomputer front-end package to access NLM's databases.

A total of 37,899 copies of Grateful Med (32,586 IBM PC versions; 5,313 Macintosh) have been distributed by the National Technical Information Service since the package was introduced in March 1986. Purchasers receive new versions at no additional cost as they become available. In FY 1991, NLM introduced Version 1.5 of the Macintosh version of Grateful Med.

In FY 1991, NLM concluded flat-rate per code pricing experiments with several institutions and is now analyzing the data gathered. The charges for online searching on NLM's system were revised to ensure full recovery of access cost. NLM now uses contract assistance to key data for new online code holders.

To provide the widest possible access to its authoritative data, NLM leases complete databases and subsets of selected databases in machine-readable form. There are now 100 organizations leasing MEDLARS data. At the end of the year, nine licensees were producing CD-ROM products containing data from six different MEDLARS databases. After considering comments and suggestions from many constituents, NLM proposed changes in revised charges for MEDLARS data in light of changes in CD-ROM and network technology and to facilitate NN/LM outreach efforts.

Reference Service and Document Delivery

In FY 1991, the Library received 66,516 requests for reference assistance, 69 percent from onsite users, 31 percent in telephone calls and less than 1 percent in letters. In addition, a large number of routine request for hours of service, directions to the Library, etc., are handled by an automatic telephone answering system. In FY 1991, NLM installed NIK (NLM Information Kiosk), an automated guide to NLM for onsite users. NIK, which is implemented in Supercard and installed on a Macintosh computer, provides information on NLM's programs and services and explains how to locate and obtain materials and reference assistance. The Library continues to upgrade and expand its internal CD-ROM network that provides access to a variety of CD-ROM tools and to the MEDSTATS expert system for locating sources of answers to statistical questions. In FY 1991, the content of MEDSTATS was revised and expanded to include sections on health care staffing, health facilities and services, costs, and general vital statistics.

NLM provides document delivery service to remote requesters as a back-up to other member libraries in the National Network of Libraries of Medicine (NN/LM) and to onsite users who wish to consult items from NLM's closed stacks. The total number of document requests submitted to NLM was 494,515, an increase of 8 percent from FY 1990. NLM received 281,606 interlibrary loan requests and filled 74 percent of them, and improvement of 3 percentage points from FY 1990. If requests for which the requester was unwilling to pay are excluded, NLM's fill rate was 81 percent. The speed with which requests are filled improved substantially; 54 percent of all filled request were processed within a single day of receipt. NLM received 84 percent of its interlibrary loan request via DOCLINE, NLM's automated request and routing system. Three percent or 7,470 requests were received via telefacsimile transfer; of these 3,728 were needed for clinical emergencies and were processed within two hours.

During FY 1991, NLM began a pilot test of the System for Automated Interlibrary Loan (SAIL) which uses scanned bit-mapped page images of selected journal titles to which NLM subscribes to fill requests referred to NLM via DOCLINE. Requested articles are printed out for mailing or converted to faxable form and sent directly without human intervention.

The number of libraries using DOCLINE increased to 2,195 in FY 1991. These libraries entered 2.1. million document requests and filled 86 percent of them. NLM filled another 8 percent for an overall fill rate of 94 percent. DOCLINE routes requests to appropriate libraries based on approximately 1.26 million SERHOLD® records, which represent the holdings of more than 3,000 NN/LM member libraries. Recent DOCLINE enhancements include a fax-only delivery option and allowance for separate bill-to and ship-to addresses.

At the end of FY 1991, Loansome Doc, a new feature of Grateful Med that allows individual health professionals to submit automated document requests to a specific NN/LM library, was available to Grateful Med users nationwide. Loansome Doc allows users to request the full text of articles identified in a Grateful Med/MEDLINE search. If a user's designated library cannot fill the request, the request can then be routed via DOCLINE. In FY 1991, Loansome Doc users requested 6,290 documents.

Onsite users requested 212,909 documents from NLM's closed stacks, an increase of 7 percent from FY 1990. Eighty-five percent of the requests were filled, and 96 percent of filled requests were delivered to users within 30 minutes. This represents a substantial improvement in service from last year. In FY 1991, NLM modified its onsite service policies to raise the daily limit on free stack requests from 10 to 12 and to impose an annual limit of 150 requests per individual. A prior analysis indicated that the use patterns of 98 percent of onsite users fell within these limits. The remaining high volume users were operating commercial document delivery services. High volume requesters may use either NLM's regular fee-based overnight photocopy service or an experimental information vendor service that was established after the change in the onsite service policy.

Special Historical Programs

The Library has an outstanding collection of rare books, manuscripts, pictures, theses, and historical pamphlets which is a unique and valuable resource to scholars throughout the world. To promote continued growth and increased used of this rich collection, NLM sponsors a number of special programs. In addition to historical research conducted by NLM staff, the Library has established a competitive Visiting Scholar Program, which invites a recognized historical scholar to spend six to twelve months at the Library. Participating scholars are expected to engage in research that will use NLM's historical collections extensively and to advise NLM staff in their areas of expertise. The Library prepares a number of historical exhibits and sponsors historical lectures and conferences each year--often in conjunction with professional associations and other government institutions. Lectures sponsored in FY 1991 included "NIH: the Crucible Years, 1930-1948" by Dr. Donald Fredrickson, former Director, NIH, and "Another Kind of Glory: Black Doctors in the Civil War" by Professor Robert Davis.

AIDS

The NLM's collection of some four million items, its MEDLARS computerized databases, and the National Network of Libraries of Medicine are the pillars of a national health information network--a network designed to ensure timely dissemination of scientific and medical information about AIDS to the biomedical community.

The Library currently sponsors three AIDS-related online databases on its MEDLARS network: AIDSLINE, AIDSDRUGS, and AIDSTRIALS. AIDSLINE is an online computer file of more than 59,000 references to the published literature on AIDS, dating back to 1980. AIDSLINE joined NLM's family of MEDLARS databases in 1988. It is updated weekly and is growing at the rate of about 1,200 new citations a month. In FY 1991, the scope of AIDSLINE was expanded to include records for relevant books from CATLINE, NLM's online catalog file, references to audiovisual programs and computer software from AVLINE, NLM's audiovisuals catalog, and abstracts from additional AIDS-related conferences, in addition to citations from MEDLINE, the Health Planning & Administration file, and CANCERLIT.

As part of a collaborative effort of the Public Health Service, NLM, in conjunction with NIAID, FDA, and CDC, provides access to information about clinical trials of experimental treatments and to information about the agents being used in those trials. AIDSTRIALS contains descriptions of over 375 investigational clinical trials currently being conducted, or completed, to test the safety and efficacy of various agents against AIDS and AIDS-related diseases. The information about the NIH-sponsored clinical trials in AIDSTRIALS is provided by the National Institute of Allergy and Infectious Diseases (NIAID), while the Food and Drug Administration (FDA) provides the information about privately sponsored trials. Included in the database is a description of each trials, eligibility criteria, and trial locations. A complementary database, AIDSDRUGS, contains descriptions of the agents being tested in these clinical trials. The information for AIDSDRUGS comes from published literature and includes adverse effects, chemical/physical properties, synonyms, and drug interactions. AIDSTRIALS and AIDSDRUGS are also available for access through Grateful Med for the Macintosh and will be included in the next release of the IBM version of Grateful Med.

The Library also publishes the monthly AIDS Bibliography--the latest in a series of AIDS "literature searches" that began in 1983. The Bibliography, with citations to journal articles and books as well as audiovisual materials, covers the spectrum of areas of AIDS concerns--preclinical, clinical, epidemiological, diagnostic, and prevention. This document can be obtained through a subscription from the Government Printing Office.

Outreach Initiative

Library Operations is contributing to NLM's special outreach initiative by gathering feedback from users and non-users of its services, by enhancing existing services to make them more useful and accessible, by developing new services to address unmet information needs, by increasing its direct efforts to publicize the Library's services, and by designing, coordinating, and evaluating outreach efforts to be carried out by the National Network of Libraries of Medicine.

In addition to speeding direct document delivery to individuals via Loansome Doc and SAIL, in 1991 NLM initiated a new online "Clinical Alert" service as part of an NIH-wide initiative to ensure that clinical trial findings with significant patient care impact are announced immediately through a variety of mechanisms. The mechanisms selected depend on the specific case and include press conferences, press releases, and use of the National Library of Medicine's online services and the National Network of Libraries of Medicine. NLM announces the significant finding through a summary "clinical alert" message on its online system, faxes or electronically disseminates the complete text of the "clinical alert" to 138 major medical libraries, and mails the complete text to more than 3,500 members of the National Network of Libraries of Medicine including libraries in hospitals nationwide. These libraries in turn disseminate the "clinical alert" to other clinical care facilities, research centers, and professional groups in their geographic areas. As of December 1991, seven clinical alerts had been distributed in this fashion to the health care community.

Library Operations has organized a greatly expanded program of exhibits of NLM's products and services at national and regional professional meetings.

NLM employees and staff from the Regional Medical Libraries will demonstrate NLM's services at a total of 44 such meetings nationwide in FY 1992. Included will be meetings with a minority focus, such as the National Medical Association, the Association of Minority Health Professional Schools, and the Inter-American College of Physicians and Surgeons.

Work has also begun on an evaluation of the first 30 individual library outreach projects that were funded by NLM in late FY 1990 and carried out to members of the National Network of Libraries of Medicine. The evaluation will look at the numbers of people reached and their subsequent use of Grateful Med and other information services. The goal is to identify successful outreach strategies for broader application throughout the country. Specific demonstration projects include a collaborative effort begun in 1990 with Meharry Medical College to test and evaluate innovative strategies to improve access to automated information systems among faculty and students on campus, and community physicians practicing in rural and inner city areas of Tennessee.

In collaboration with the University of Texas Health Science Library in San Antonio, a circuit librarian program serving remote and largely Hispanic counties in the Rio Grande Valley underwent evaluation in 1991 to assess the feasibility of extending the reach of a professional librarian to remote hospitals and health clinics where medical librarian services are otherwise unavailable. Along similar lines, a major outreach initiative is being developed by NLM to extend library services and access to clinically relevant computer databases among care givers practicing in the lower Mississippi Delta, a 214 county/seven state region, characterized as the most impoverished area of the nation.

Health Services Research

In 1989, NLM received a legislative mandate to work with the newly created Agency for Health Care Policy and Research (AHCPR) to improve information services in the field of health services research. With funds provided by AHCPR under an interagency agreement, the Library established an Office of Health Services Research Information (OHSRI) and initiated a number of activities to improve access to health services research information and to support the development of AHCPR-sponsored clinical practice guidelines.

In FY 1991, NLM reviewed and revised its selection policy for health services research literature and expansion of the NLM collection in this area is already underway. With the help of a joint NLM/AHCPR Task Force, the Library has begun to revise and expand Medical Subject Headings (MeSH) terminology in the field of health services research. A substantial number of new concepts and cross-references were added to MeSH for 1992 as a result of this effort. A more specific publication type "Practice Guideline" was created to allow more precise retrieval of these important documents.

To date, the NLM staff has provided extensive literature search support and back-up document delivery service for nine different panels convened by AHCPR to develop clinical practice guidelines. Other Network libraries have provided primary document delivery service to some of the panels. NLM is establishing several mechanisms to facilitate access to AHCPR-sponsored guidelines once they are approved. Electronic copies of some versions of the guidelines will be available for automatic document delivery. NLM's Lister Hill Center is also developing an online system that will provide access to the full-text of AHCPR approved clinical practice guidelines.

At the end of FY 1991, NLM received from the Institute of Medicine (IOM) a report entitled "Improving Information Services for Health Services Researchers: A Report to the National Library of Medicine." The report recommends expansion of NLM's existing services, development of some new services--a database of available datasets that are useful in health services research--and training for medical librarians to assist them in responding to the complex information needs of producers and users of health services research. In the coming year, the Library will develop plans and resource estimates for carrying out recommended activities that are not already underway.

Lister Hill National Center for Biomedical Communications

The Lister Hill National Center for Biomedical Communications (LHNCBC) is the primary computer research and development arm of the National Library of Medicine. Center projects develop and apply new computer and information science methods to organize and provide access to the enormous quantity of knowledge in the life sciences, whether found in words, pictures, sounds or laboratory measurements. Research projects conducted and supported by the Center include applications of computer technology as varied as the development of computer programs that can not only process knowledge but acquire it themselves for use by researchers in their research decision-making, to the representation in three dimensional electronic images of human anatomy for more accurate instruction of health professions students.

Under the High Performance Computing and Communications initiative, the LHNCBC will undertake several new efforts: first, a "Visible Human" project to construct a digital library representing the x-y-z numerical coordinates of complete human beings at millimeter level resolution; second, development of a system which can store and transmit radiology images over the National Research and Education Network; third, the LHNCBC will accelerate development of the Unified Medical Language System, a project to develop tools to establish links among the various sources of computerized biomedical information. These projects are described in greater detail below.

Computer Based Educational Resources

The newest educational resources project is the development of a digital image library of a complete male and female human form. This "Visible Human" project will create a computerized three dimensional representation of the entire body, as derived from computerized tomography (CT), magnetic resonance imaging (MRI), as well as photographic sections of selected human cadavers. Such a library will provide an unparalleled opportunity to create computer programs and systems which demonstrate the complexities of human internal anatomy in a manner which allows the user to selectively rotate, "dissect", and reassemble organs, tissues, and body regions on the computer screen.

Recent developments in interactive computer-based learning at NLM include a videodisc and microcomputer program on cardiac imaging, produced in collaboration with Dr. Carl Jaffe of Yale University, and an interactive videodisc which teaches methods of screening for cervical cancer, produced in association with the National Cancer Institute. A composite videodisc containing excerpts from over 20 other computer-based teaching programs was completed, as a "technology sampler" to acquaint medical faculty with the possibilities of the electronic medium for health professions education.

Digital X-ray Prototype Network (DXPNET) Project

In cooperation with the National Center for Health Statistics (NCHS) and the National Institute of Arthritis, Musculoskeletal and Skin Diseases (NIAMS), the LHNCBC is supporting the National Health and Nutrition Examination Surveys (NHANES) which periodically produce statistics on the health status of the U.S. population. The LHNCBC contribution to NHANES will be a system which transmits digital representations of the x-rays acquired in the survey, using wide area high speed computer networks. A total of 27,000 x-rays will be stored in electronic format on optical disc at LHNCBC, and made available to researchers nationwide via the NREN. LHNCBC is currently building and testing a prototype low cost workstation that enables technicians from NCHS to perform quality control on the images produced by scanning the x-rays.

Unified Medical Language System

The UMLS® project was initiated in 1986 as a long-term NLM research and development effort designed to facilitate the retrieval and integration of information from multiple machine-readable biomedical information sources. The sources of interest include: descriptions of the biomedical literature, clinical records, databanks, knowledge-based systems, and directories of people and organizations. The variety of vocabularies and classifications used in these different sources is a significant barrier to the use of machine-readable information by health professionals and biomedical researchers and to the development of effective search interfaces to assist these users. The UMLS approach assumes continued diversity in the terminology employed in different systems and by users themselves. The goal of the project is to develop products that can be used to connect users to the machine-readable information relevant to their questions, irrespective of these differences in terminology.

In FY 1991, NLM released the 2nd Experimental Edition of the UMLS Knowledge Sources. This 2nd edition includes updated versions of a Metathesaurus™ of more than 220,000 terms from several biomedical vocabularies and classifications and a Semantic Network of the sensible relationships among the broad semantic types or categories to which all concepts in the Metathesaurus are assigned. It also includes the first version of an Information Sources Map that describes the content and access conditions for biomedical databases in both "human-readable" and machine-readable form. The initial Information Sources Map describes 50 nationally available databases including all those available from NLM. The UMLS Knowledge Sources are designed primarily for use by system developers. They are meant to be consulted and used by search interface programs to interpret user inquiries, to select databases with relevant information, and to formulate searches in the terms appropriate to the selected databases.

Expert Systems Program

A research program in artificial intelligence concentrating on expert systems was established at LHNCBC in 1984. Expert systems are computer programs which combine knowledge of a particular subject area with inferencing mechanisms enabling them to use this knowledge in problem-solving situations. There are two basic types of expert systems: Systems which help experts in dealing with too much information, and systems for the transfer of an expert's knowledge. The latter systems allow access to an expert's knowledge and can make it available and understandable when the human specialists are not. Systems of both types are under active development at the Lister Hill Center.

The Expert System Program continues development and evaluation of the AI/RHEUM consultant system in rheumatology, one of the world's largest medical artificial intelligence systems. AI/RHEUM is the best known of a series of knowledge-based medical consultant systems using the criteria table form of knowledge representation pioneered by NLM researchers. The power, simplicity and flexibility of this representation are augmented by a new expert system shell written at NLM for the development of criteria-based reasoning systems. In its current state, the AI/RHEUM diagnostic system contains in its knowledge base information on 32 rheumatologic diseases. It reasons from nearly a thousand patient findings (basic information such as signs, symptoms, laboratory tests and radiographic observations). It has several hundred text definitions available in a fraction of a second to explain those patient findings which might not be familiar to its intended users. In addition, the system offers direct access to a "Show Me More" videodisc image bank illustrating specific rheumatologic findings which contains 6,300 still frames and 15 minutes of motion video sequences to help physician users accurately make patient observations otherwise difficult to illustrate.

Natural Language Systems Project

Natural Language Systems (NLS) research is focussed on the representation and understanding of human language within computers. The many technical "dialects" found in the life sciences create special requirements for language understanding, and the research questions lie at the intersections of the fields of biology, medicine, computer science, and linguistics and involve methods and approaches used in all of these fields. A major emphasis of the project is the development of SPECIALIST, an experimental systems for parsing, analyzing, and accessing biomedical text. NLS staff members have recently begun the in-depth analysis of a sample of MEDLINE abstracts with the goal of establishing criteria for the automated analysis of the information structure of biomedical abstracts.

System for Automated Interlibrary Loan (SAIL) Project

The System for Automated Interlibrary Loan or SAIL Project involves both electronic document preservation and delivery to support the NLM's interlibrary loan (IL) service. The system is creating an electronic image store on optical disc of page images of selected journals in the NLM collection. It will then provide automated access to page images on optical discs for telefacsimile ("faxing") or reproduction for documents, linked to NLM's DOCLINE interlibrary loan system.

After development and implementation of a pilot system limited to 61 journal titles and the start of online document delivery, the program will generate cost and throughput data for decisions on the wider implementation of this new technology. The electronic capture system has been developed and is now being evaluated and refined. Such systems have the potential to augment bibliographic searching with speedy and automatic document delivery via electronic methods.

In April of 1991, the prototype System for Automated Interlibrary Loan became operational. Beginning with page images from 60 selected journals, the system grew to contain over 100,000 pages by late 1991. SAIL automatically responded to interlibrary loan requests for over 96% of the journal articles which it contained and provided 2-8% of NLM's overall interlibrary loan journal service throughout the latter half of 1991.

Outreach Initiative

As part of NLM's outreach efforts, the Lister Hill Center program has developed an intramural Undergraduate Research Study Program to provide two-year scholarships and research assignments in medical informatics for sophomore students majoring in electrical engineering, computer science, computer engineering, or physics at participating historically black colleges and universities (HCBUs). The program will includes 3 schools that will participate with NLM for a five year-period. Participating students will complete two summer internships at the Lister Hill National Center for Biomedical Communications and two academic year assignments under the guidance of their academic preceptors.

National Center for Biotechnology Information

The rapid pace of progress in biotechnology and molecular biology presents a challenge to computer and information science to collect, analyze, and make available an ever-increasing body of knowledge. The National Center for Biotechnology Information (NCBI) was established in 1988, as a division of the National Library of Medicine specifically to facilitate the dissemination of information that is so critical to understanding the molecular processes that control health and disease.

The NCBI not only creates the databases for storing and analyzing knowledge in genetics and molecular biology, but as part of the NIH intramural program it performs basic and applied research of advanced methods of understanding the structure and function of biologically important molecules. A group of over 30 senior scientists, postdoctoral fellows, and technical staff work in the areas of molecular biology, genetics, biochemistry, structural biology, mathematics, and computer science. In the past year NCBI scientists have made significant contributions to the discovery and analysis of new human disease genes. NCBI software and databases were critical elements in the identification of the neurofibromatosis-1 gene, the analysis of familial colon cancer genes, and the determination of the coding region for the Kallmann syndrome gene.

Beginning in September, 1992, the NCBI will assume the responsibility for building and distributing the NIH's GenBank database, the foremost collection of all known DNA sequences. NCBI has been working closely with the National

Institute of General Medical Sciences (NIGMS), who has managed the database since 1982, to insure an efficient transition. NCBI, in collaboration with the Library Operations Division of NLM, has been building sequence records from the over 3400 journal articles indexed for MEDLINE at the NLM. These records will be supplemented with data directly from authors which will be processed by the Los Alamos National Laboratory under an interagency agreement.

The NCBI-GenBank database will be significantly enhanced with the addition of protein sequences and MEDLINE citations, and by becoming an element in an integrated database that will link specialized databases together to provide users with seamless searching across a wide range of molecular data. NCBI is working with other NIH institutes, academic groups, and Federal agencies such as the National Science Foundation, Department of Energy, Department of Agriculture and the U.S. Patent and Trademark Office (USPTO) to insure that all federally supported molecular sequence data are incorporated in this database which is already a vital resource for biological research, including the Human Genome Project.

Equally important as capturing molecular sequence data is the ability to access and retrieve the information using automated systems. NCBI's extensive program in software development has created tools that end-user biologists can use to solve their research problems such as a single CD-ROM disk which includes over 90,000 sequences with associated MEDLINE abstracts that can be searched from a Macintosh or PC. Over 600 copies of the CD-ROM are in use in biology laboratories and libraries. The software tools used to create and access data on the CD-ROM are being freely distributed to the biology community as well as to academic and commercial software developers. Searching tools are also being developed for use over the Internet or National Research and Education Network (NREN). A sequence search program, known as BLAST, is being employed by the leading genome research groups and enables them to compare a new, unknown sequence against over a hundred thousand sequences in seconds and to have the results returned instantly over the network. With over 500 searches performed per day, the BLAST network service is recognized by research groups as an essential laboratory tool to not only analyze data but to aid in setting directions for new research.

As part of its mandate to support the development of new information technologies of relevance to biology and genetics, the NCBI has exercised a leadership role in sponsoring forums for the exchange of information among leading scientists from the fields the computer science and biology. A Visitors Program has been established and brings members of the scientific community to the NCBI to engage in collaborative research in bioinformatics. Workshops on sequence analysis have been presented to the NIH campus and to outside groups such as USPTO patent examiners. Additional information dissemination is being provided by the GenInfo Data Repository, a network-based service for distributing software and databases produced by the NCBI as well as outside groups.

High Performance Computing and Communications

The NCBI employs high-performance computing resources and high-speed networks to support its own research and to provide analysis services to outside users. Modeling of protein structures and prediction of their structures are computationally intensive problems and require hours or days of computing time. As part of the database preparation work, classification and comparison of sequences are performed in order to assist researchers by grouping similar classes of sequences together. These calculations essentially compare the database against itself and require days of compute time even on parallel machines. The use of high-performance computing is critical in this area of research and specific examples of gene identification over the past year have corroborated the need for continuing to increase computing power and storage to cope with the volume and complexity of data.

The specific problems which require high-performance computing include molecular sequence analysis which involves searching against hundreds of megabytes of data, molecular modeling which despite sophisticated algorithms and classification methods still consumes hundreds of CPU hours for structure searches, and network search and retrieval services. Extensive work is also underway on advanced text retrieval methods since such a large component of experimental biology information is textual. Statistical text retrieval methods have been developed at NCBI that measure document similarity and cluster groups of like documents for fast retrieval and browsing.

Toxicology Information Program (TIP)

The Toxicology Information Program, a major activity of the Division of Specialized Information Services, has worked closely with the toxicology community through the aegis of the Toxicology Information Program Committee (TIPCOM). TIPCOM, an advisory committee, managed by the National Academy of Sciences (NAS), is comprised of distinguished scientists representing such fields as chemistry, pharmacology, toxicology, environmental health and safety, medicine and computer sciences.

The Program's long-established chemical and toxicological databases provide an enormous storehouse of references and data on the health and environmental effects of hazardous substances. NLM's Toxicology Data Network (TOXNET) has proven a successful approach to offering online numerical and factual data about chemicals and their effects. The Hazardous Substances Data Bank (HSDB) -- one of the databases on TOXNET -- is also being used in providing information in chemical emergency response situations, e.g., in responding to highway spills involving hazardous substances.

A number of databases have been developed as TOXNET components in collaboration with other agencies such as the National Institute of Environmental Health Sciences (NIEHS), the Environmental Protection Agency (EPA) and the Agency for Toxic Substances and Disease Registry (ATSDR).

The increasing public concerns about the impact of ubiquitous chemicals on the public health and the environment has created a critical need for factual information in Federal and State agencies. Such agencies are looking upon the NLM online information systems as ideal vehicles to search and retrieve data in such areas as toxicology, hazardous materials, occupational and environmental health, and the basic biomedical sciences. TIP is ready to meet this challenge and will maintain its strong ties with the scientific community while broadening its services to Federal, State and local governments, academia, industry and to the general public.

Long Range Planning

As a continuation of the NLM Long Range Plan, a Long Range Planning Panel on Toxicology and the Environment was convened, for the first of three planned meetings in November 1991, to (1) review the current products and services provided by the Toxicology Information Program, and (2) recommend future roles for the National Library of Medicine in this area. The Panel has representation from other Government agencies, public advocacy groups, industry, academe, and health care providers. Working Groups will address, in greater detail, issues such as databases in other organizations, international information resources and activities, users and their needs, database building, and the information needs of responders to chemical emergencies. The report and recommendations of the Panel will be presented to the NLM Board of Regents.

TOXNET and its Files

The TOXNET computer system and its files constitute one of the world's most comprehensive sources of information on the health and environmental effect of hazardous substances. During 1991, the TOXNET system underwent a complete software conversion to the MUMPS computer language and an entirely new hardware implementation. Transparent to the users, a networked microprocessor-based system in a mirrored architecture became publicly available on May 6. Specifically, the initial configuration of the TOXNET network consisted of ten 33 Mhz 386-based microprocessors with over 13 gigabytes of online disk storage and 224 user ports on three terminal servers. Since the microprocomputer network was released in May, the system has already grown by the addition of two more microprocessor for search/retrieval; three more developmental processors; and one more terminal server. Upgrades have included the capability of linking TOXNET to INTERNET.

Major features of the new microprocessor network include: (1) a load balancing capability of directing new users to the least loaded processor for more efficient use of system resources; (2) a separate microprocessor which serves as a system monitor to ensure optimum operation; (3) rapid journaling capabilities to obviate the need to perform periodic copies from the database servers; and (4) uninterruptible power supplies to protect the system and ensure continuous power. This new system has demonstrated increased performance with mirrored copies of all databases. Yet, the Library expects to save close to $400,000 annually when compared to the continued growth path of the previous minicomputer system.

The Hazardous Substance Data Bank (HSDB) continues to be supported, in part, by the Agency for Toxic Substances and Disease Registry (ATSDR) and the NLM. HSDB contains data on over 4,200 chemicals relevant to human and animal toxicity, biomedical effects, safety and handling, human exposure, environmental fate, and other areas. Recent enhancements include the addition of summary sections for human/animal toxicity and for chemical hazards in addition to the environmental fate summaries already in the records. Concept menu searching for the occasional or novice user has been fully implemented during this past year. HSDB is the most heavily used file on TOXNET.

The Toxic Chemical Release Inventory (TRI) series of files is mandated by the Emergency Planning and Community Right-to-Know Act (Title III of the

Superfund Amendments and Reauthorization Act of 1986). These files, compiled and maintained by EPA, contain data collected from industry on the amounts of 328 specified chemicals released to the environment (air, water, soil) or transferred to waste sites. A file containing the data reported to EPA for 1989 was made available on TOXNET in the Spring of 1991. Special TOXNET search capabilities have been developed for TRI including: (1) menu searching; (2) ranging of data; (3) sorting of retrieved information; (4) capabilities for manipulating numerical data; and (5) cross-file searching for multiple-year files of TRI.

The Chemical Carcinogenesis Research Information System (CCRIS) continues to be maintained by the National Cancer Institute (NCI) and deployed by NLM on TOXNET. This data bank contains test results from carcinogenicity, genotoxicity and tumor promotion studies that have been evaluated and published in the scientific literature. Tumor inhibition studies were made available in the past year. CCRIS now contains 3,262 records.

The Registry of Toxic Effects of Chemical Substances (RTECS) is a data bank, derived from a National Institute for Occupational Safety and Health (NIOSH) file by the same name, which NLM restructures for online searching in TOXNET. RTECS now contains nearly 110,000 records. In FY 1991, new data were added to RTECS to report some toxicology testing where high doses had shown no effect.

The Integrated Risk Information System (IRIS), a file developed and maintained by EPA, became available on TOXNET in March 1990 and has become the third most heavily used file in this short period of time. IRIS contains EPA health risk and regulatory information on 590 chemical substances. IRIS risk assessments are prepared for both carcinogens and noncarcinogens via oral and inhalation routes of exposure. The data undergo a high level of review by EPA scientists.

The Environmental Mutagen Information Center (EMIC) bibliographic database contains citations to publications concerned with the evaluation of agents for genotoxic activity. EMIC is produced by the Human Genome and Toxicology Group of the Oak Ridge National Laboratory, a Department of Energy (DOE) contractor, under an interagency agreement between NLM and the DOE. EMIC is funded by the National Institute of Environmental Health Sciences and the Environmental Protection Agency. NLM assumed management of the database in 1987 and is now responsible for the building, maintenance, and public access to it via the TOXNET system. The current file, EMIC, will become publicly available in FY 1992. EMICBACK, the backfile for EMIC, became available on TOXNET in FY 1989. EMICBACK contains over 70,000 citations to literature published from 1950-1991.

The Developmental and Reproductive Toxicology (DART) database has been available on TOXNET since May 1990. DART, a bibliographic database, is comprised of citations to publications concerned with teratology--birth defects--and to a lesser extent, other areas of reproductive and developmental toxicology. Over 10,000 citations to literature published since 1989 are found in DART, with approximately 3,600 citations being added each year. DART is a continuation of the Environmental Teratology Information Center (ETIC) database. These older citations are available on TOXNET as the ETICBACK database. ETICBACK contains over 49,000 citations to literature published from 1950-1989.

DART is funded by the Environmental Protection Agency and the National Institute of Environmental Health Sciences and managed by the NLM. NLM and the funding agencies are working together to expand the scope of DART to include additional aspects of developmental and reproductive toxicology, such as infertility and the effects of neonatal and childhood exposure to toxicants. The Teratology Information Users Group, an outside advisory group of scientists and physicians, is assisting NLM in developing the content of the DART database.

The GENE-TOX file was added to TOXNET in February, 1991. The file, created and maintained by EPA, contains peer-reviewed data on genetic toxicology for 3,000 chemicals. Each test system in the online file has been reviewed by a committee of scientists and is referenced with citations to original source papers and the official GENE-TOX panel report publication.

Databases Under ELHILL

ChemID (Chemical Identification File) is an online directory file made available on the NLM computer system in February 1990. It contains over 195,000 records of important biomedical and regulatory substances, and provides access to these records at normal MEDLINE user charge rates. For a given chemical substance, the ChemID record provides identifying information such as Chemical Abstracts Service Registry Numbers and a variety of chemical names. It also points users to other NLM databases containing information about the chemical in question. ChemID also provides a link to selected lists maintained by key regulatory and scientific organizations. This collection of list searching capabilities is known as SUPERLIST. SUPERLIST allows answers to such questions as: Is a given chemical on the U.S. Department of Transportation or on the U.S. Environmental Protection Agency's RCRA list, or the International Agency for Research in Cancer (IARC) list.

In 1991, ChemID was rebuilt to add more components to SUPERLIST such as the Priority-based Assessment of Food Additives (PAFA) file, a list of food additives from the Food and Drug Administration. Data from the European Inventory of New or Existing Chemical Substances (EINECS), were also added to ChemID, providing valuable information about chemicals reported to the European Community.

CHEMLINE (Chemical Dictionary Online) is an online chemical dictionary and directory file containing records for chemical substances cited in NLM databases. The main function of CHEMLINE is to assist the user in searching bibliographic and other databases for biomedical and toxicological information about chemical substances. Thus, for a given substance, CHEMLINE provides Chemical Abstracts Service Registry Numbers, molecular formulas and chemical names. Each CHEMLINE record also directs the user to NLM databases containing information about that substance. Originally made available in January 1974 with about 59,000 records, the file now contains over 1 million records describing chemical substances of biomedical or regulatory interest. It is available on NLM's ELHILL system with a royalty surcharge added to NLM's user charge rates because of the extensive use of data in CHEMLINE that are obtained under license from Chemical Abstracts Service.

During FY 1991, CHEMLINE was completely regenerated and updated bimonthly to keep it current with the NLM files for which it provides locator information. The format of the file was also changed to be more consistent with the easy-to-use format used by the new ChemID file. Important generic names such as United States Adopted Names (USAN) for drugs are now separated from other chemical names for the convenience of the searcher. Data from the Pharmacological Action and MeSH Scope Note fields of the NLM Medical Subject Heading (MeSH) file were also added to CHEMLINE records, giving users valuable additional information about the biomedical usage of key chemicals.

TOXLINE (Toxicology Information Online) is an online bibliographic retrieval service produced by merging "toxicology" subsets from some seventeen secondary sources. The TOXLINE files continue to be updated monthly and regenerated annually, and are structured so that TOXLINE and its backfile, TOXLINE65, contain data only from sources which do not require royalty charges based on usage. Information from Chemical Abstracts, which does involve such usage royalties, is used exclusively to maintain two other online files, TOXLIT and TOXLIT65. During FY 1991 the FEDRIP subfile in TOXLINE of toxicology-related research projects was replaced with a more current version. In addition, a new subfile which will expand TOXLINE information on teratogenicity was prepared, and development of a new subfile of research projects supportive of risk assessment activities in several Federal agencies was begun.

The four databases in the TOXLINE/TOXLIT family now contain over three million records, representing more than a ten-fold increase in the number of records since the original TOXLINE file was first made available by NLM in September 1972. Several other vendors now license portions of these databases for either online or CD-ROM distribution, thus increasing access to this storehouse of toxicological information.

DIRLINE (Directory of Information Resources Online) is an online directory of over 18,000 information and service resources. These resources range from voluntary health organizations able to supplement the information health professionals provide to patients, to NIH-supported scientific facilities that are available for the use of biomedical researchers. DIRLINE is composed of a variety of subfiles, generally produced and maintained by other agencies. The kind of information provided by DIRLINE is not readily available from bibliographic databases. Since the National Referral Center of the Library of Congress, one of the major subfile producers, has discontinued its database, NLM will be assuming direct responsibility for the content of a large portion of DIRLINE.

Outreach Initiative

A new initiative by NLM's Toxicology Information Program is aimed at establishing a mechanism that would strengthen the capacity of Historically Black Colleges and Universities (HBCUs) to train medical and other health professionals in the use of toxicological, environmental, and occupational information resources provided by NLM. This audience represents a group that might otherwise not get exposure to these valuable information sources and also is considered one of the high priority groups within NLM's widespreading outreach efforts. Pilot training programs are being developed at nine universities. These institutions have been provide with training in the use of NLM information services. They were loaned PC-based workstations containing instructional software as well as a user-friendly access tool (Grateful Med)), and they are being given free access to the NLM databases for a period of one year. This pilot project is being guided by a newly-developed Toxicology Information Outreach panel composed of one representative from each of the nine participating HBCUs, three representatives directing training activities at other Government agencies, and two consultants.

Microcomputer-Based Training Products

The development of microcomputer-based training programs for the CHEMLINE, ChemID, TOXLINE, and MEDLINE databases began in 1986. The first version of CHEMLEARN, a training package for CHEMLINE, was released in the Fall of 1987, and a significantly enhanced version was released in the Fall of 1988. MEDTUTOR and TOXLEARN, microcomputer-based training programs for MEDLINE and TOXLINE respectively, were released in the Summer of 1989. These programs provide easily accessible, inexpensive alternatives to formal classroom training. In 1990 a microcomputer-based training program for the ELHILL software, ELHILL LEARN, was released. It was designed as a front-end to the CHEMLEARN, TOXLEARN, and MEDTUTOR programs. While it is primarily intended for new users unfamiliar with the ELHILL software, it can be used as a quick reference tool to reinforce or recall previously-learned search techniques. In 1991, the TIP Demo Disk was repackaged in a Windows 3.0, multimedia format. It incorporates audio -- voice and music -- extensive graphics, and animation. Currently, TOXLEARN is being repackaged in the same Windows 3.0, multimedia format as part of the National Library of Medicine's Toxicology Information Outreach Project.

Health Hotlines

Health Hotlines, a booklet listing approximately 300 toll-free telephone numbers of health-related organizations that provide information or services, has been widely distributed and has proven to be extremely popular. Since NLM receives hundreds of requests for this publication each month, NLM would like to distribute the next version of Health Hotlines through the General Services Administration's Consumer Information Catalog as part of the Library's outreach effort.

Workstation for Response to Chemical Emergencies

With the support of the Emergency Response Team of the Agency for Toxic Substances and Disease Registry (ATSDR), NLM's Toxicology Information Program has built a microcomputer workstation that provides information needed by responders to emergencies involving hazardous chemicals. A subset of NLM's Hazardous Substances Data Bank (HSDB) augmented with emergency medical information and other relevant files has been placed on a CD-ROM disk and stored in the workstation to allow for local searching. The workstation has also been linked to a service that provides National Weather Service information online. This facilitates decision-making when the dispersion of fumes or clouds of gases, resulting from a chemical spill, is a problem. Through a fax capability built into the workstation, retrieved and reformatted information can be readily transmitted from the command center which houses the workstation to emergency vehicles at the accident site. All these capabilities have been packaged into a microcomputer that was field-tested in FY 1991, by State health departments and poison control centers at 15 sites around the country. The field test showed that ANSWER is fully functional in a command center environment where it increased the availability of information to emergency responders and served as a useful record keeping tool concerning the accidents to which the center responded.

Information Services to Other Agencies

NLM's Toxicology Information Program (TIP) continues to provide information services to the Agency for Toxic Substances and Disease Registry (ATSDR) in support of their legislative mandates. NLM also maintains and deploys supportive systems of data and information sponsored by various Federal agencies.

TIP provides the Deputy Chair, as well as scientific and committee management support for the Subcommittee on Information Coordination (SIC) of the Department of Health and Human Services' Committee to Coordinate Environmental Health and Related Programs (CCEHRP). TIP staff also represented NLM on numerous interagency committees and working groups, such as CCEHRP's Subcommittees on Risk Assessment Research Resources, the National Toxicology Program's Working Group on the Annual Report on Carcinogens, and the Interagency Task Force on Environmental Cancer, Heart and Lung Disease. Recently, NLM, through TIP, took on the formation and co-chairmanship of the Database Working Party of the FCCSET (Federal Coordinating Council for Science Engineering and Technology) Subcommittee on Risk Assessment.

National Library of Medicine

Research Management and Support

Authorization Legislation - Sections 301, 465-467 of the Public Health Service Act. 1993 Authorization: Indefinite

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
98	$7,443,000	108	$8,177,000	108	$8,531,000	--	+$354,000

Research Management and Support funds the salaries and expenses of the staff who provide for overall administration and direction of the National Library of Medicine programs, including the extramural grant and contract programs. Among functions carried out in this activity are execution of basic administrative services; contracts processing and management; grants management and the scientific direction of NLM's extramural programs, financial and personnel management; coordination of equal employment opportunity activities; direction of NLM's international programs; public inquiries and management of the Library's publications; and operations research. NLM's planning and evaluation activities are also provided for in this activity.

Funding for Research Management and Support during the last 5 years has been as follows:

	Amount	FTE
FY 1988	$6,274,000	91
FY 1989	6,294,000	87
FY 1990	6,940,000	96
FY 1991	7,443,000	98
FY 1992	8,177,000	108

Rationale for Budget Request

The FY 1993 budget request for Research Management and Support is $8,531,000 and represents an increase of $354,000 above the FY 1992 appropriation. Through this activity, NLM will continue to provide efficient and effective administrative support and management, and scientific direction for its programs.

ICD: National Library of Medicine

Detail of Permanent Positions

	1991 Actual	1992 Appropriation	1993 Estimate
ES-5	1	1	1
ES-4	4	4	4
ES-3	1	1	1
Subtotal	6	6	6
GS/GM-15	29	29	29
GS/GM-14	42	42	42
GS/GM-13	76	76	76
GS-12	117	118	118
GS-11	52	52	52
GS-10	2	2	2
GS-9	34	34	34
GS-8	22	22	22
GS-7	61	61	61
GS-6	37	37	37
GS-5	22	22	22
GS-4	18	18	18
GS-3	2	2	2
Subtotal	514	515	515
Grades established by act of July 1, 1944 (42 U.S.C. 207):			
CO-6	3	3	3
CO-5	1	1	1
CO-4	1	1	1
Subtotal	5	5	5
Ungraded	1	1	1
Total permanent positions	526	527	527

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Advisory and Assistance Services

In FY 1993 NLM's consultant services requirements total $286,000, an increase of $11,000 from the FY 1992 for anticipated mandatory increases. NLM utilizes consultant services in a number of functional areas as part of the continuing efforts to define and address the information needs of the medical community. Consultant services are utilized to obtain advice and assistance in very specialized areas.

The largest component of the consultant services funds is for advisory services of the Toxicology Information Program Committee (TIPCOM) of the National Academy of Sciences for NLM's Toxicology Information Program (TIP). TIPCOM reviews current TIP activities and provides advice on assessing and planning for the intermediate and long range goals of TIP.

NLM also utilizes consultant funds to obtain special expertise and consultation in areas such as literature collections and preservation, software development, and medical expert systems evaluation methodology development.

Advisory Committee expenses are also included in planned consultant services for continued funding of NLM's Board of Regents, the Lister Hill National Center for Biomedical Communications Board of Scientific Counselors, National Center for Biotechnology Information Board of Scientific Counselors and Library Operations' Literature Selection Technical Review Committee.

NLM's internal controls for consultant services ensure that only those consultant services that are necessary and approved are procured. NLM programs are required to specify specific consultant services needs during the budget review process conducted by the Director of NLM. The Director approves the level of consultant services to be utilized. His decisions are then used as a basis to develop an annual consultant services plan and determine the level of a separate budgetary allotment for consultant services. The planned and actual obligations charged to that are utilized to monitor consultant services obligations.

Thursday, March 26, 1992.

JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES

WITNESSES

DR. PHILIP E. SCHAMBRA, DIRECTOR, FOGARTY INTERNATIONAL CENTER

DR. BERNADINE P. HEALY, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. RICHARD M. KRAUSE, SENIOR SCIENTIFIC ADVISOR, FOGARTY INTERNATIONAL CENTER

ROBERT B. EISS, DIRECTOR, OFFICE OF INTERNATIONAL SCIENCE POLICY AND ANALYSIS, FOGARTY INTERNATIONAL CENTER

H. RICHARD MILLER, EXECUTIVE OFFICER, FOGARTY INTERNATIONAL CENTER

ELLA L. MENSER, BUDGET OFFICER, FOGARTY INTERNATIONAL CENTER

DENNIS P. WILLIAMS, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTRODUCTION OF WITNESSES

Mr. Natcher. At this time we take up the budget request for the John E. Fogarty International Center for Advanced Study in the Health Sciences.

We have before the Committee, Dr. Philip E. Schambra.

It is a pleasure to have you before the Committee at this time.

Before you give us your statement, tell us who you have with you.

Dr. Schambra. Thank you, Mr. Chairman. It is a pleasure to be here.

At my far left is Ms. Ella Menser, Budget Officer; next to her is Mr. Robert Eiss, Director of the newly-formed Office of International Science Policy and Analysis; and Mr. Richard Miller, Executive Officer.

To my right is Dr. Richard Krause, Senior Scientific Advisor, and to his right Dr. Healy and Mr. Williams from the Department.

Mr. Natcher. Now, Dr. Schambra, we will be glad to hear from you.

Opening Statement

Dr. Schambra. Thank you, Mr. Chairman.

If I may, I would like to submit my complete statement for the record and provide a shortened version of it for you this morning.

The Fogarty International Center was established due to the far-sighted vision of Representative John Fogarty and his congressional colleagues who envisioned, quote: "At Bethesda a great international center for research in biology and medicine dedicated to international cooperation in the interests of the health of mankind."

What Mr. Fogarty envisioned has come to pass. As the Center enters its 25th year, new discoveries in science and new breakthroughs in medicine depend upon cooperation with our international partners. Science has become a global enterprise.

The Fogarty Center plays a central role in convening experts and marshaling resources from around the world to seek the causes of disease and develop methods of treatment and prevention.

The Center's AIDS International Training and Research Program has established linkages with institutions in developing countries, and is training a cadre of investigators from those countries to conduct future collaborative vaccine trials to combat this worldwide epidemic. The program also contributes to the creation of an international sentinel network of investigators, who are poised to detect and prevent the spread of future disease outbreaks before they become global emergencies.

The Center employs broad-based fellowship and exchange programs and regional initiatives in Central and Eastern Europe and Latin America and the Caribbean to promote the interchange of new ideas and scientific knowledge.

Mr. Chairman, I am very pleased to note that our regional initiative in Eastern Europe—especially our new, small research grant program—has been cited by the National Academy of Sciences as a model for other agencies to follow. And we were highly gratified to receive a cable earlier this month from our Ambassador in Czechoslovakia, Mrs. Shirley Temple Black, from which I would like to quote.

It reads as follows: "Sciatt"—that is the embassy's science attache—"has received several very laudatory comments on the Fogarty Center's Central and Eastern European Initiative (CEEI) from the Czechoslovakia Academy of Sciences and from individual scientists. The outreach programs to support scientists from the region, provide training in advanced research methods in the U.S., to fund short-term visits to explore/develop/conduct research, to provide essential research equipment, and to convene research development workshops is focused precisely on the areas of greatest immediate need. This program should be continued, and should be given high priority for follow-on funding."

It is signed, Ambassador Black.

Mr. Chairman, I am pleased to report that over the past year, scientists supported by the Fogarty Center contributed to advances in: development of vaccine approaches to HIV/AIDS, malaria, and childhood respiratory diseases; high resolution magnetic resonance imaging to visualize the chemistry of bone formation; development of gene therapy techniques; and DNA sequencing technologies to map the human genome.

Major progress was made toward discovering the causes of osteoporosis, hypertension, diabetes mellitus and viral-based cancers, among other national and international public health priorities. And later this year, we will sponsor the first World Congress on Tuberculosis to energize a global effort against the reemerging scourge.

As the focus for NIH international efforts, the Fogarty Center coordinates international programs and policies at the interagency level. In fiscal year 1991, we led an interagency biodiversity initiative to identify potential new drugs from natural products. We also led activities of the White House Federal Coordinating Council on Science, Engineering and Technology, FCCSET, Committee on International Science, Engineering and Technology to provide guidance to the Administration on S&T relations with the European Community and Eastern Europe.

As our Center enters its 25th year, the most serious challenge facing the U.S. scientific community is to maintain excellence and global leadership. The Fogarty International Center will continue to develop creative and innovative programs which advance American science and bring to the American public the best dividends that derive from medical research wherever it occurs—improved health for all.

Mr. Chairman, our fiscal year 1993 budget request is $20,727,000. I will be pleased to answer any questions you may have.

[The statement of Dr. Schambra follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement of the Director
John E. Fogarty International Center for Advanced Study in the Health Sciences

The Fogarty International Center (FIC) was established as a result of the far-sighted vision of Representative John Fogarty and Congressional colleagues who envisioned "at Bethesda a great international center for research in biology and medicine dedicated to international cooperation in the interests of the health of mankind." As the Center enters its 25th year, I would like to express our gratitude to Congress for its guidance and commitment to the programs of the FIC.

Twenty-five years ago, medical science was on the eve of a new era. Scientists had learned to observe and manipulate biological events in living organisms down to the smallest components--the individual molecules--the bricks and mortar of life. This achievement resulted from a collaborative effort on the part of American and foreign scientists. Well known are the achievements of James Watson, an American, and Francis Crick, an Englishman, who discovered the molecular structure of DNA, the heredity material of our genes. A consequence of this earlier effort is the human genome project, which has become an international enterprise that will have profound implications for biology and medicine. Important discoveries have already been made through international cooperation in human genetics. Scientists have identified the genetic markers for Huntington's chorea, Down syndrome, and cystic fibrosis. These studies are expected to lead to a new generation of therapies that will reverse the disease process at the genetic level. For example, French Anderson and his colleagues at NIH are collaborating with counterparts in Holland, France nd Italy to refine gene therapy techniques.

It is noteworthy that in the last 25 years twenty percent of the Nobel prizes awarded to American scientists were shared with foreign scientists. The evidence is overwhelming that the conduct of biomedical and behavioral science has become an international enterprise. NIH has defined its international character by investing in scientific pursuit worldwide, for the benefit of the American people as well as the world community.

The capacity of the United States to benefit from scientific opportunities and new discoveries will increasingly depend on cooperation between our scientists and their foreign colleagues. This situation is attributable to global developments that offer new opportunities and new challenges. These include: the rapid spread of infectious disease across national borders and the potential for new epidemics to arise; increasing opportunities to study populations and environments in formerly closed parts of the world; growing foreign investment in biomedical research and the rapid growth of highly innovative scientific laboratories abroad; the establishment of global information and communication networks; and the emergence of an international market for research investment and scientific employment.

FIC plays a central role in convening experts and coordinating resources worldwide to develop the research strategies for the diagnosis, treatment and prevention of diseases. For example, the FIC AIDS international training and research programs, based in 11 U.S. schools of medicine and public health, have trained 400 foreign scientists and public health workers from 49 countries, including those from the newly opened countries of Eastern Europe and the Commonwealth of Independent States. Over 100 training courses have been held, reaching more than 4,500 health care workers and technicians worldwide. Now in its fourth year, this is the largest global research training effort to combat HIV/AIDS. The program has trained an international cadre who are prepared to join with their American colleagues in joint ventures on AIDS vaccine and drug trials. The development of an HIV/AIDS vaccine will require testing in regions of the world where the incidence of the disease is high and where geographic differences in the genetic composition of the virus and transmission of the disease necessitate local field trials.

The FIC AIDS training and research programs are also contributing to the creation of an international sentinel network of basic and clinical investigators who are prepared to detect and prevent new disease outbreaks before they become international emergencies. It is important to note that although the HIV/AIDS epidemic has demonstrated the difficulties of coping with a new infectious disease, it is but one of several new or newly recognized infectious diseases which have emerged in recent decades due to rapid and continuing social and ecological change in tropical regions. For example, we are currently working closely with our sister agencies of the PHS to develop international strategies to combat the unexpected recurrence of tuberculosis.

FIC's capacity to meet the challenges of changing world conditions is also exemplified by its regional initiatives in Eastern Europe and in Latin America, which were implemented in FY 1990. In FY 1992, FIC has launched a new program of supplemental research grants to NIH-supported scientists whose domestic-based studies would benefit from collaboration with scientists in these regions.

Specifically, scientists are studying geographic differences in the prevalence of hypertension and diabetes among Black populations in the U.S. and the Caribbean to better understand genetic and environmental risk factors for these disorders. Research groups from Hungary and Czechoslovakia are developing, in cooperation with their American colleagues, novel techniques for separating DNA fragments in order to improve our capacity to map the human genome. Polish and American scientists are measuring environmental pollution to determine if pollution is a risk factor to the developing fetus.

Research supported under FIC fellowship programs spans the breadth of biomedical investigation and contributes to research areas which have been identified as priorities at the NIH. In the emerging field of molecular medicine, for example, an FIC research fellow from France working at the Salk Institute has developed a strain of transgenic mice that will provide a new experimental model for diabetes mellitus. The work is based on new research that implicates altered immunity as a risk factor for diabetes. Such research is necessary, if we are to discover the cause and thereby prevent diabetes in humans.

Research conducted by an American research fellow in Germany has resulted in new diagnostic screening methods to distinguish between infantile and adult types of metachromic leukodystrophy, a genetic disease that causes blindness and dementia. The researchers have been successful in correcting an enzyme defect in human cells grown in the laboratory, with the objective being to develop successful gene therapy to correct this inherited disease.

In a search for the causes of osteoporosis, which often strikes post-menopausal women, an American senior fellow at Oxford University is investigating the chemistry of bone formation and resorption, a process that occurs in osteoporosis. Visualization of these steps in bone chemistry with high resolution magnetic resonance imaging is the first step toward developing targeted drugs to prevent and arrest the effects of osteoporosis.

In the field of vaccine development, a Fogarty Scholar from England working at the NIH has developed a novel vaccine strategy by employing viruses that infect bacteria, but are harmless to humans. These viruses are genetically modified so that they contain bacterial substances that stimulate immunity in animals during preclinical testing. In collaboration with NIH scientists, research is underway to use this strategy to develop vaccines against HIV/AIDS, malaria, and childhood respiratory diseases.

A Scholar from Sweden working in the field of neuroscience and behavior has identified genes that regulate the formation and function of peptides that influence the cognitive, sensory and motor functions of the brain. Elucidating these regulatory processes is the basis for understanding the biochemical nature of neurological and behavioral disorders and the future development of effective treatment and intervention.

As the focus for international efforts at the NIH, the FIC coordinates international programs and policies at the interagency level and links NIH with other international components of the Department of Health and Human Services (DHHS), the White House Office of Science and Technology Policy, the Department of State, the Agency for International Development and other federal agencies, as well as foreign agencies and multilateral and international organizations. In FY 1991, FIC provided the federal lead for a new interagency biodiversity program to identify potential new anti-cancer and anti-viral drugs from natural products and to help preserve the rich natural diversity of the world's rain forests and oceans. The broad objective of this initiative, which FIC will administer, is to promote both economic growth and ecological conservation by demonstrating the value of biological resources from which natural products are derived.

The FIC also represents the DHHS on the Committee on International Science, Engineering and Technology (CISET), established under the Federal Coordinating Council on Science, Engineering and Technology. I continue to serve as Vice Co-Chairman of the CISET, which provides government-wide policy guidance on international science and technology issues and serves as a mechanism for interagency planning and coordination. FIC staff have led CISET activities to guide the Administration on Science and Technology relations with the European Community and the new democracies of Eastern Europe.

As FIC enters its 25th year, the most serious challenge facing the U.S. scientific community is to maintain excellence and global leadership. The FIC will continue to develop creative and innovative programs which further global leadership and bring to the American public the best dividends that derive from medical research wherever it occurs--improved health for all.

Thank you Mr. Chairman. The FIC budget request before you for FY 1993 is $20,727,000. I will be pleased to answer any questions you may have.

CURRICULUM VITAE

Name:	SCHAMBRA, DR. PHILIP E.	
Date & Place of Birth:	November 8, 1934. Saginaw, Michigan	
EDUCATION:	1956 -	B.A., Rice University
	1961 -	Ph.D., Yale University
	1961-1963	Postdoctoral, Institut fur Strahlenbiologie, Karlsruhe, Germany
	1964-1966	Postdoctoral, University of California, Berkeley

Professional History:

1956-1958	Research Assistant, Biophysics Department, Yale University.
1958-1961	Predoctoral Fellow, National Cancer Institute, Biophysics Department, Yale University.
1961-1963	Research Associate, Institut fur Strahlenbiologie, Karlsruhe, Germany.
9/64-2/65	Instructor, Department of Medical Physics, University of California, Berkeley.
1964-1967	Research Biophysicist, University of California, Berkeley.
1966	Laboratory Director, National Science Foundation Summer Institute in Radiobiology, University of California, Berkeley.
1967-1968	Grants Associate, National Institutes of Health.
1968-1971	Budget Examiner, Office of Management and Budget, Executive Office of the President.
1971-1974	Staff Member, Council on Environmental Quality, Executive Office of the President.
1974-1980	Associate Director for Interagency Programs, National Institute of Environmental Health Sciences, NIH.
1980-1984	Chief, International Coordination and Liaison Branch, Fogarty International Center, NIH.
1984-1988	Science Attache and PHS International Health Representative, U.S. Embassy, New Delhi, India.
1988-Present	Director, Fogarty International Center, National Institutes of Health.

Honors and Awards:

1989	PHS Superior Service Award
1982-1991	Outstanding Performance Ratings
1986-1988	Merit Performance Awards
1984	NIH Merit Award
1987	Secretary DHHS Certificate of Appreciation
1964-1966	NASA Research Fellowship, University of California, Berkeley

GLOBALIZATION OF SCIENCE

Mr. **Natcher**. Thank you, Dr. Schambra.

Now, Doctor, the budget documents refer to the "globalization of science." If you will now, explain what you mean by that phrase and tell us how important this change is as far as NIH is concerned.

Dr. **Schambra**. Mr. Chairman, what this means is simply an observation of the basic fact that science, as it has developed today in all fields, not just biomedicine, but all fields, is global in nature. It has been observed by a number of leading scientists over the past century: there is no such thing as national science. It is international in nature.

That is particularly true in biomedicine where we have to be concerned about diseases that arise at home and abroad as well. I think the AIDS virus is a perfect example of the globalization of biomedical science. It is a problem that has arisen abroad, but one we must deal with on a global scale in order to contain it.

INTERNATIONAL CHANGES AND OPPORTUNITIES

Mr. **Natcher**. In your personal opinion, Doctor, do you believe NIH has done enough to take advantage of international changes and opportunities?

Dr. **Schambra**. Sir, I think that the decision by President Johnson and the Congress to establish the Fogarty International Center was indeed a wise one. The strong support that our Center has had over the years—now going into our 25th year—is an example of the commitment the Administration and the Congress have made in order to take advantage of and build on the opportunities that exist internationally.

I feel that with the budget we have we are able to take advantage of those opportunities and will continue to do so in the future.

FUNDING IN FOREIGN COUNTRIES

Mr. **Natcher**. Last year you testified that a larger portion of NIH's resources should be spent in other countries. It has been just above 1 percent historically. Will this increase in 1992 and 1993?

Dr. **Schambra**. The latest data that we have developed is for 1991. There we have about a one-tenth percent increase over the previous year, fiscal year 1990.

Over the many years we have been collecting this data it has been about 1.5 percent. We saw modest increases in fiscal year 1991. I think it is too early to tell at this point whether the percentage will increase in 1992 or 1993, but certainly I would expect any increase to be in proportion to the overall NIH budget.

INTERNATIONAL COMPONENT OF STRATEGIC PLAN

Mr. **Natcher**. Was the issue of raising NIH's international commitment discussed as a specific policy option when NIH developed its draft strategic plan?

Dr. **Schambra**. Indeed, it was, sir. We had very strong support from the leadership of the NIH Institutes and especially from Dr.

Healy for bringing out the international dimension of all of the NIH programs.

In fact, as one reads through the strategic plan as it stands now, in all the elements of the plan reflecting the international character of biomedical science today, the international dimension is there.

HUMAN FRONTIER SCIENCE PROGRAM

Mr. NATCHER. The budget materials describe a new Human Frontiers Project, which is jointly financed with other countries. What can you tell us about how this research is organized?

Dr. SCHAMBRA. The Human Frontier Science Program is a very innovative initiative that was proposed by the Japanese Government—the Prime Minister of Japan—at the Venice Economic Summit in 1987.

The purpose of the program is to support international collaboration in molecular and cellular biology and brain research. The program is headquartered in Strasbourg, France, and is under the direction of an international committee consisting of the representatives of the countries in the economic summit and the European Community.

The program awards research grants and fellowships and provides support for a modest number of conferences. I might point out that in the period from 1990 to 1992, the program awarded 98 research grants, 35 of which, or 36 percent, were awarded to projects led by American scientists.

The total value of those projects was over $57,000,000. During that period of time, the program also awarded 300 fellowships. Nearly 60 percent of the fellows chose to work in the U.S.

During the initial period of this program, the last three years, the total funding was $74,000,000, with 91 percent of the funds provided by Japan.

As we move into the next phase of this program, all of the participating countries have agreed it is now time for them to make contributions to the program. The Administration has decided that the United States will contribute $3,500,000 to the program beginning in fiscal year 1993, pending the consent of the Congress, of course.

The NIH has made a commitment to contribute a total of $1,000,000 of that amount, of which $500,000 will come from the Fogarty Center, if the budget is approved as presented.

Mr. NATCHER. What is the total cost of the Human Frontiers effort and what portion will be financed by each country, Doctor?

Dr. SCHAMBRA. The level of funding currently is approximately $35,000,000 a year.

As I mentioned, up until now the funding has come predominantly from Japan, well over 90 percent. But as we move into the next phase, an increasing amount, but still a very small fraction as it adds up, will come from the other countries. The United States, pending consent of Congress, will contribute $3,500,000, about 10 percent of the program's budget.

The British have made a commitment of about $600,000. The French and Germans are providing some cash and in-kind support, and Japan will provide about $30 million.

FOREIGN FUNDING OF BIOMEDICAL RESEARCH

Mr. NATCHER. Beyond this specific project, how active are other countries such as Germany and Japan in supporting biomedical research internationally including the United States?

Dr. SCHAMBRA. That is quantitatively a very difficult figure to obtain. We do know from the contacts we have had with the Germans, for example, that they provide support for a large fraction of American scientists studying in Germany. I think Dr. Krause has those figures.

Do you recall Dr. Krause?

Dr. KRAUSE. I don't have the exact number but, in fact, at least 4,000 or 5,000 Americans are studying in Germany in the various sciences, most supported by the various agencies of the German government.

Dr. SCHAMBRA. We will try to develop that information for you and for the record, Mr. Natcher.

[The information follows:]

We have information on international expenditures in health research for several countries, which my staff has gathered through consultations with research institutions abroad. In 1991, the British Medical Research Council expended approximately $350 million in 1991 on health research. An estimated two percent of this amount, or $7 million supported international activities. The German Ministry of Research and Technology provided $370 million in health research support in 1991. An estimated 4 percent of this amount, or $14.8 million supported international activities. The French National Institute of Health expended approximately $365 million on biomedical research in 1991, an estimated 8 to 12 percent of this amount was expended on international activities.

NIH support for scientific pursuit worldwide has provided models for health research programs of other countries and has enhanced research investments of foreign governments. Our colleagues at the German Ministry of Research and Technology advise us that the example of NIH has deeply influenced federal support for health research in Germany. The NHLBI outreach programs for prevention of high blood pressure, for example, have been adapted throughout Germany with new program investments at the federal and state levels. Also, many of our formal agreements with other countries stimulate new funding from foreign governments for cooperative research activities.

Mr. NATCHER. Mr. Pursell, I yield to you.

FIC NATIONAL AND INTERNATIONAL PRIORITIES

Mr. PURSELL. Welcome, again.

Could you describe for me your top priorities?

Dr. SCHAMBRA. Mr. Pursell, we have a number of priorities, but I would say that overall, both for the Fogarty Center and representing all of the components of NIH in their international priorities, our first priority is to build linkages between the best scientists abroad and American scientists to be sure that the research discoveries that are developed abroad find their most rapid application and incorporation into medical treatment and research programs in the United States.

Mr. PURSELL. Give us an example of how you do that. What would your role be?

Dr. SCHAMBRA. One of the ways is through our Senior International Fellowship program where we select some of the best mid-career medical scientists to go abroad.

This can be up to three separate terms within a 3 year period, if justified by the research proposal they are presenting. The aim is to get them into the best foreign laboratories.

When we look at the statistics of where they go, we find they are consistently going to the best laboratories in the U.K., and Western Europe.

Mr. PURSELL. What would be your other priorities?

Dr. SCHAMBRA. This would be a qualitative description of our number one priority. There is no question about it.

In terms of more specific priorities we need to expand our collaboration with scientists in Latin America, Eastern Europe, and now recently in the former Soviet Union, to take advantage of the opportunities for scientific collaboration that have occurred through the democratization process that these countries have gone through.

Mr. PURSELL. Are there more Soviet scientists available for work in the U.S.?

Dr. SCHAMBRA. We have seen participation by former Soviet scientists in the intramural research program at NIH increase from less than five to today over 60.

Mr. PURSELL. We have about 60?

Dr. SCHAMBRA. Working in the Institutes at NIH, that is correct.

You asked about priorities, we would like to expand these regional initiatives now to cover areas of the world where we don't have active programs, particularly Africa and Asia.

Building on our AIDS research and training programs we would like to be able to expand our efforts into dealing with the problem of emerging diseases. The AIDS virus is an excellent example of an emerging disease that spreads to become a global disease. We see cholera coming back, with four thousand dying from cholera in Latin America last year, and we are also seeing a reemergence of tuberculosis.

Mr. PURSELL. Is that the international focus?

Dr. SCHAMBRA. Those are the examples.

Mr. PURSELL. How about your priorities as an agency? Can you give me a couple more?

Dr. SCHAMBRA. I mentioned our programs that are involved now in preparing scientists to test therapeutics and vaccines against HIV and AIDS in foreign countries. This should be expanded and involve other new and emerging pathogens, such as those I just mentioned.

We feel there is more we can do in promoting the participation of American minorities in the Fogarty programs. That becomes an important priority as well.

Mr. PURSELL. Does it make a difference if we are in the continental U.S.? Is that agenda different from an international agenda?

For example, AIDS is an international matter. Are there other diseases and problems that the United States sees as a high priority.

Dr. Schambra. I think, as far as the developing countries of the world go, the disease priorities would be parallel. The principal causes of morbidity and mortality in the United States, cardiovascular diseases and cancer, are the same.

Mr. Pursell. In my State, we are number one in chronic diseases. Our priority is not so much the HIV problem, as it is the problem of chronic diseases.

We try to do a parallel of the needs of the State versus the United States. How do you balance it off?

I am trying to focus on where that proper balance should be.

Dr. Schambra. That is a good question, how one balances the two. We clearly have our feet in both camps. We support the disease priorities that are important to American scientists by funding applications we get to our fellowship programs. The Senior International Fellowship program for American scientists going abroad is largely active in the developed countries in the world.

The major priorities are biotechnology, molecular biology, cancer, and cardiovascular diseases. These are both international and national priorities.

Mr. Pursell. How do you reach an agenda of deciding the priorities of other countries?

Dr. Schambra. These are priorities of the American scientific community. The Fogarty Center has the ability to point out opportunities that may not be pursued as well in the developing countries of the world. Here is where our AIDS program provides a special way to be able to get involved in those health issues and research topics which may not be pursued as emphatically based on domestic priorities but are still important to us internationally.

WORLD HEALTH ORGANIZATION

Mr. Pursell. What if you were to disagree with the World Health Organization's agenda or the White House's agenda of science and technology. Where do you fit?

Dr. Schambra. In the case of the World Health Organization, WHO, every year we get a chance on behalf of the NIH, to review in detail the WHO program and budget. Our Institutes are involved in that review too.

A delegation, usually with NIH representation and headed by the Secretary of this Department, attends the annual meetings of the World Health Organization. I have represented NIH on this delegation for the last four years.

Mr. Pursell. Would there be a lot of negotiating going on? Is that part of the process?

Dr. Schambra. At the WHO level, there is certainly a lot of give and take on that. When necessary, there are votes taken and a decision is made on a majority basis.

INTERNATIONAL LEADERSHIP

Mr. PURSELL. What is the image of the United States in terms of international leadership?

Dr. SCHAMBRA. I would say it is exceptionally high. The United States, largely through the National Institutes of Health—and I am pleased to say for the last 25 years through the Fogarty Center—has been a major supporter of international collaboration in biomedical science. This began at a time when much of the rest of the world, was recovering from the 2nd World War. All nations have benefited from NIH's leadership in the post-war period.

Mr. PURSELL. Are there any countries who are not carrying their fair share financially?

You mentioned Japan as being a more aggressive leader.

Dr. SCHAMBRA. We are working very actively to encourage other countries to make an even greater contribution to international science and technology cooperation. Over the past 10 years or so, we have persuaded a number of countries to initiate programs to support American scientists to study abroad, including Japan.

Mr. PURSELL. What kind of support?

Dr. SCHAMBRA. Full support.

Mr. PURSELL. Are France and Germany, Mexico, Canada and others involved?

Dr. SCHAMBRA. The Western European countries are generally very supportive of international collaboration. A large number of American scientists find support in their laboratories.

Mr. PURSELL. Are they very supportive in helping us with the underdeveloped nations as well?

Dr. SCHAMBRA. Yes, they are.

Mr. NATCHER. Mr. Early?

Mr. EARLY. Doctor, I find your statement as interesting as any we have had before this Committee.

I want to acknowledge my good friend, Dr. Krause. When he was Director of the Institute of Allergy and Infectious Diseases, he did as good a job as anyone who held that position.

Dr. KRAUSE. Thank you, Mr. Early.

TRAINING PROGRAMS

Mr. EARLY. I think this is a vehicle for saving millions of dollars for the Federal Government. I think we could make substantial cuts in our foreign aid program, where we spend money to buy foreign policy.

You are requesting $19,000,000. You say, in your statement, that French Anderson, who I have great respect for, and his colleagues are working with scientists in Italy and Amsterdam on gene therapy.

You say that the Fogarty Center plays a central role in coordinating resources worldwide for the diagnosis and treatment of diseases. You speak about examples; the Fogarty Center's international aid, international training and research programs, based at 11 medical schools. You have trained 400 foreign scientists and health workers from 49 countries?

Dr. SCHAMBRA. That is correct.

Mr. EARLY. If we want foreign countries to respect us, isn't that what it is all about?

Dr. SCHAMBRA. Yes, sir, I would say it is.

BIODIVERSITY INITIATIVE

Mr. EARLY. I understand you are planning a new initiative in biodiversity. Can you tell us what that is all about and what the Fogarty Center's role will be in that?

Dr. SCHAMBRA. Yes, sir, I will be pleased to.

This is a new initiative based on discussions we initiated about a year ago with a number of agencies including the National Science Foundation—which is interested in the topic of biodiversity preservation—and the Agency for International Development—which is interested in economic development in developing countries where many of these rare species of plant and marine life are found. The National Cancer Institute and NIAID are interested in the development of products that may have action against cancer or the AIDS virus.

We agreed in a series of meetings to combine our interests and resources and to create a new program to be co-funded by NIH, NSF, and USAID. This program would develop centers abroad, particularly in developing countries, to train people to search for plants that have bioactive products. They would be trained to preserve the environment in which those species exist. The Centers would also be concerned about protecting the economic interests of the regions in which new bioactive products are found.

That is basically is the essence of the program.

HUMAN FRONTIER SCIENCE PROGRAM

Mr. EARLY. Fine.

Doctor, I was extremely interested in a response you gave to the Chairman. The budget request before us includes $500,000 for something called the Human Frontier Science Program. Is that what you have in this budget?

Dr. SCHAMBRA. That is correct, sir.

Mr. EARLY. You told Mr. Natcher this program is $35,000,000 annually.

Dr. SCHAMBRA. That is the current estimate.

Mr. EARLY. It is easy to be critical of Japan, but you said 95 percent of the money is coming from Japan?

Dr. SCHAMBRA. It has been 91 percent. Over the Program's first three years, of its $74,000,000 total budget, 91 percent has been contributed by the Japanese Government.

Mr. EARLY. In your statement you indicated that in the last 25 years, 20 percent of the Nobel Prizes awarded to scientists were shared with foreign scientists; is that correct?

Dr. SCHAMBRA. That is correct.

SUPPORT FOR SOVIET UNION SCIENTISTS

Mr. EARLY. The Fogarty Center has such potential. Unlike Chairman Natcher, who spoke about him, I was not lucky enough to know John Fogarty.

We are hearing a lot about the need to rescue science in the former Soviet Union. Is the Fogarty Center doing anything in that area?

Dr. SCHAMBRA. Yes, we are trying under the circumstances to be as helpful as possible. You will recall that we began our Central and Eastern European Initiative in 1990, using reprogrammed funds. The program was expanded in 1991 and further expanded in 1992 with about $700,000 from the $1,000,000 increase in our budget which you appropriated for the CEEI and the Latin American and Caribbean Initiative. Because of the circumstances, the completely-changed circumstances in the Soviet Union, we decided to extend the Central and Eastern European Initiative to include the republics of the former Soviet Union, as well as the Baltic States.

So we have been able, with funding of about $500,000 last fiscal year, and in excess of $800,000 in the current fiscal year, to promote collaboration specifically between American and former Soviet Union scientists.

We have also, through our new small research grants award, called the FIRCA Program, made the first round of awards in which proposals for cooperation with Russian scientists have been very successful. This small grants program has been highly appreciated by foreign scientists, as mentioned in the cable from our Ambassador to Czechoslovakia.

There was an article in the Washington Post today about yesterday's House Science Committee hearings. According to the article, the Committee heard from Russian scientists pleading for deals with the United States. They asked for cooperation, not aid, and insisted they have much to offer despite the country's economic plight. That is what we are doing, offering cooperation, not aid.

Mr. EARLY. The Russian people are smart people.

If they get some health and nutrition programs, and they get some assistance from our Fogarty Center, which is funded at less than $20,000,000, what is their long-range perception of the United States going to be in your opinion, Doctor?

Dr. SCHAMBRA. I think if we can provide an adequate level of support that will promote scientific cooperation along the lines recommended by our National Academy of Science just this last week, I think it will have a long-term, very significant impact not only in the diplomatic relationships between our countries, but in terms of the scientific relationships and the benefits we will derive as well.

TUBERCULOSIS

Mr. EARLY. Earlier, we heard about problems that we are having with tuberculosis in this country. Is the Fogarty Center doing anything with other countries about things they can be doing with regard to tuberculosis?

Dr. SCHAMBRA. Absolutely. We have been planning and will hold in November this year, the first World Congress on Tuberculosis. We are holding it here in Washington.

Mr. EARLY. The work that the Center is doing with foreign countries on AIDS, on hypertension and diabetes, that is the type of activity that any Member of Congress can be proud of. That is spending less than $20,000,000.

If we provide the fund $20,000,000, we would be telling other countries, those in like Africa, which have specific AIDS problems, we could help to educate their public health people.

I want to commend you and your Institute. I personally appreciate your statement very much.

Dr. SCHAMBRA. Thank you very much, Mr. Early.

Your words are music to my ears.

FOGARTY INTERNATIONAL RESEARCH COLLABORATION AWARD (FIRCA)

Mr. NATCHER. Now Dr. Schambra, your only major increase in the 1993 budget appears to be $750,000 additional for Fogarty International Collaboration Awards. How many additional awards will be made, Doctor?

Dr. SCHAMBRA. Mr. Natcher, altogether we will increase our Fogarty International Research Collaboration Awards from an estimated 19, in this fiscal year, to 47 in 1993, under the current budget.

FY 1993 BUDGET REQUEST

Mr. NATCHER. Are there any other significant increases or decreases which the subcommittee should be aware of, Doctor?

Dr. SCHAMBRA. Between 1992 and 1993, we anticipate an increase of about $72,000 to support the NIH Visiting Program, that is the support that we give to the Institutes that bring foreign scientists to work at the NIH, as well as $500,000 for the Human Frontier Science Program.

We expect a decrease of about $150,000 in conferences and workshops and a $278,000 decrease in our support for the International Research Fellowship Program.

STAFFING

Mr. NATCHER. The 1992 budget included 10 additional full-time equivalents for your center. Have these positions all been filled, Doctor?

Dr. SCHAMBRA. No, they have not been all filled at this point.

Mr. NATCHER. Can you tell us how many have been filled?

Dr. SCHAMBRA. As of the end of February, we had filled 72 positions.

Mr. EARLY. Mr. Chairman, would you yield?

Go right ahead.

Mr. EARLY. Can you tell us why you have not filled those positions?

Dr. SCHAMBRA. We are doing our best to recruit staff for the positions. One of the positions, for example, is a senior program officer who will be responsible for our collaborative programs with Japan.

We are hoping to find somebody who has personal knowledge of the scientific enterprise in Japan and speaks Japanese. It is difficult to find somebody with all of those skills.

Mr. NATCHER. Now, Doctor, the 1993 request as you know, includes two more positions.

What grade level will they be and how will they be used, Doctor?

Dr. SCHAMBRA. One position, an International Health Program Officer, will be at about the GS–13 or 14 level, and the second position, a Program Assistant, will be at the GS–5 or 6 level. Both of these positions are associated with the Biodiversity Initiative I described to Mr. Early, and both positions will be reimbursed by the other agencies participating in the program.

At this point, the Fogarty Center will not be putting any resources into the Biodiversity Initiative other than its administrative skills and international contacts and will be totally reimbursed by the other participating agencies.

AIDS-RELATED ACTIVITIES

Mr. NATCHER. How much of your 1993 budget request is for AIDS-related activities?

Dr. SCHAMBRA. $5,849,000 is identified as AIDS-related dollars.

Mr. NATCHER. Other than training, which you discussed in your statement, what is the main involvement in the Fogarty Center in the AIDS area?

Dr. SCHAMBRA. I think if we were to go through our various fellowship programs, for example, the International Research Fellowship Program that brings foreign scientists to the United States, I think we would find a few of those fellows doing research related to AIDS, and other STD's, and closely associated problems such as tuberculosis. I think we would also find some senior American fellows involved in that topic.

All of our AIDS trainees are involved in AIDS-related research and some of our Eastern European fellows are involved in AIDS research as well.

PERSONNEL COMPENSATION

Mr. NATCHER. The object class schedule on page 148 is pretty straightforward with one exception. Your 1993 estimate of personnel compensation increases by 17 percent. With only two new positions, why are these costs increasing by 17 percent?

Mr. MILLER. Mr. Natcher, the 1992 appropriation column reflects our current anticipated needs for personnel compensation, and includes adjustments for reimbursable compensation from a number of reimbursable interagency and intra-agency agreements.

Not knowing what the future will bring with these types of reimbursable agreements, we have to project full personnel costs in the budget. If we do realize reimbursements from other agencies, we redirect that money into our other program areas, such as our reprogramming of funds in FY 1990 to start the Central and Eastern Europe and Latin America and Caribbean Initiatives.

HISTORICAL PATTERNS OF DISEASE

Mr. NATCHER. Before concluding the hearing, Dr. Schambra, I want to ask Dr. Krause—and, Doctor, it is a pleasure to have you back before our Committee at any time—a question.

Doctor, you have been an historian now of infectious diseases over the centuries. Some years ago, you published an excellent book, and I have a copy of it, on this topic, called The Restless Tide. As you look at the recent outbreak of AIDS, tuberculosis and other infectious diseases, Doctor, how do you see the situation? Are we seeing a dangerous shift in the historic patterns with these diseases? Where are we, Doctor? How do you feel about it?

Dr. **Krause**. Thank you, Mr. Natcher, for your kind remarks.

Let me be very brief. Yes, I think there have been some changes in the last 15 years that have resulted in an acceleration in the infectious diseases that face us.

First of all, there is more rapid migration of people. There have been armies on the move. There have been changes in the ecology with farm hands pushing into rain forests where they get exposed to diseases that the farmers had not previously been exposed to.

All of these things, the changes in what we do and what we are doing in the world, have, if you will, turned up microbes and given them new opportunities they have not had before.

We see because of global travel and international communications, diseases such as dengue now rampant in Latin America and several hundred million cases of malaria occurring per year. Both of these diseases are spread by mosquitoes. They can spread to the South Pacific and to the United States, as the mosquitoes exist there. Fortunately, they have not done so yet. We also know about the resurgence of cholera, which also poses a threat to the U.S. The next thing is that microbes, like humans can constantly evolve in the evolutionary stream. New ones can come just as AIDS has done. Others have come as well. We had Korean hemorrhagic fever at the time of the Korean War.

We must remain alert, alert around the world, in communication with our colleagues around the world, so that when we know what is going on, we could conceivably have the opportunity to stop things before they happen.

I might say that one of the real accomplishments through international cooperation of science, through the cold war with China and Russia, was the constant pursuit of a better flu vaccine. Influenza has been called the slippery disease because it has the ability to change its overcoat and escape our vaccines. But by constantly having the surveillance around the world, for example knowing that Hong Kong or Asian flu is on the rise, we have changed the vaccine.

It is a challenge. I think we have done it with the flu and other diseases. I think we will do it with AIDS. But Mother Nature will have something else in store for us down the road, and we better be prepared with what this Committee has given us for research to stem the tide.

Might I just make a further comment, though? There is one chapter of that book that I am proud of. It is on Florence Nightingale. She is thought, oftentimes, to be the person who started modern nursing—and she did.

More than that, she was a brilliant woman. She was one of the first people to see the importance of applying mathematics to the analysis of medical data so it was rigorous. I must say the male surgeons and physicians did not do a very good job at that.

She saw the importance of that. She had been trained in mathematics. She analyzed her data with mathematical analysis that has lasted the test of time.

You were kind to bring up my book, so I wanted to mention that.

Mr. PURSELL. I sponsored the bill to create the Institute for Nursing, so I am proud to hear about that.

I, too, along with Joe, appreciate the role this Center can have. I think the potential is great. I would prioritize the underdeveloped nations if I were in your shoes.

Speaking for myself, I think the Committee does appreciate your leadership.

Dr. SCHAMBRA. Thank you very much.

Mr. NATCHER. Mr. Early.

Mr. EARLY. I have no further questions.

Mr. NATCHER. Dr. Schambra, we want to thank you and your associates for appearing before our Committee at this time on behalf of your budget request for fiscal year 1993. It has been a good hearing.

[The following questions were submitted to be answered for the record:]

Questions Submitted by the Subcommittee

SUB-SAHARAN AFRICAN

Mr. Stokes: Last year, we discussed briefly Secretary Sullivan's trip to Africa. Based on the findings of this trip, it appears that this area provides tremendous opportunities for our nation in a variety of health areas. To what extent is the institute supporting scholar exchange programs with Sub-Saharan Africa?

Dr. Schambra: The Fogarty International Center has been actively involved in the support of collaborative research and training for scientists from Sub-Saharan Africa under its AIDS International Training and Research Program. A total of 117 African scientists from 16 African countries have received advanced research training in the U.S. and 33 in-country training courses were provided for over 1,000 health scientists in nine African countries in such areas as epidemiology, prevention and treatment of AIDS. Much of this has been concentrated in those Sub-Saharan African countries heavily impacted by AIDS such as Uganda, Malawi, Tanzania, Rwanda, Kenya, and Zambia. Among the research topics under study by African scientists are studies of the role of breast feeding in the transmission of HIV-1 in Zambia; studies of clinical risk indicators for maternal-fetal transmission of HIV-1 in Tanzania; studies of the effect of HIV infection on the protective effect of BCG vaccinations in Uganda; and studies of the neurodevelopment of children born to seropositive mothers in Rwanda. The FIC will continue to emphasize collaborative studies with African scientists in the reannouncement for the second five-year funding cycle of its AIDS programs.

Mr. Stokes: What other efforts do you plan to undertake to strengthen your activities in this area?

Dr. Schambra: We are currently exploring with other NIH components the possibility of co-funding collaborative research, workshops and other cooperative efforts in FY 1992 or FY 1993 to enhance U.S.-African collaboration on health problems of mutual concern.

As we discussed last year, the FIC has developed a proposal for an African Initiative to address childhood diseases and other public health priorities. This initiative is designed to promote cooperation among American and African scientists and institutions to develop and test new and improved medical technologies and prevention strategies that address health problems of common concern. Advances in recombinant DNA technology have accelerated the rate of vaccine development and hold promise for new and improved vaccines against diarrheal, respiratory, sexually transmitted and parasitic diseases. Research on immunization techniques has also created new approaches to recombinant-based diagnostics and therapeutics. Many of these emerging medical technologies will require parallel studies in the U.S. and regions of the world where there is a high concentration of infected individuals.

Due to the disease burden throughout Sub-Saharan Africa, cooperation with African institutions--from basic investigations to field research--would accelerate efforts to bring effective new public health tools to Africa, the U.S. and the global community. In addition, unique opportunities could be pursued to explore the etiology of diseases and disorders prevalent among African-Americans, including hypertension, sickle cell anemia, and diabetes mellitus. Expanded cooperation would also improve Africa's indigenous capacity to apply new and existing knowledge to public health priorities and to develop science-based national public health programs.

While we view this as an important effort, no explicit funding is identified within the FY 1993 President's budget to implement this initiative at this time. However, as I noted earlier, we are exploring the possibility of co-funding some activities with other components of the NIH.

Mr. Stokes: Also, what role can the U.S. play in strengthening the impact of U.S. health, population and nutrition assistance to Africa?

Dr. Schambra: I believe that a crucial corollary to health, population and nutrition assistance to African nations is a commitment to the longer term needs of building research capacity. Many immediate needs exist in areas of primary care, for example, which must be addressed through medical assistance programs. However, our ultimate goal should be to transfer the basic and clinical research skills necessary for African scientists to assess their health and population problems in the future and join as equal partners in the international effort to advance public health.

The Commission on Health Research and Development, representing major international assistance agencies, has recommended that donor-assisted health projects in developing nations should commit at least 5 percent of project budgets to research capacity strengthening and research activities.

HIV/AIDS

Mr. Stokes: I understand that the institute's AIDS international training program, now in its fourth year, is the largest research training effort to combat HIV/AIDS. Describe some of the activities which are being supported in this area.

Dr. Schambra: The program provides both long and short-term training in the U.S., as well as short-term in-country training. Through the first three years nearly 400 foreign health scientists from nearly 50 countries have received training in the U.S., and over 100 in-country training courses have been conducted which benefitted more than 4,500 health professionals in 20 countries. Over $10.5 million have been expended during the first 3 years of the program.

A few examples of the research conducted through the AIDS program include:

A Fogarty postdoctoral fellow from Zambia, at the University of Miami, in collaboration with a Fogarty fellow from Haiti, has completed an analysis of the safety and tolerance of AZT in a clinical population of children with AIDS. The hypothesis was that AZT can be safely administered to community-based pediatric patients with a minimum amount of clinical and laboratory follow-up to monitor toxicity. Preliminary analysis indicated that the frequency of clinical adverse effects possibly related to AZT in this population was no greater than the frequency of these events noted in the Phase II Pediatric ACTG trial of AZT. One fellow is also playing a key role in compiling data for the International Registry of HIV-1 Exposed Twins in collaboration with scientists from the National Cancer Institute. The fellow from Haiti, upon return to his country, is collaborating with colleagues from Johns Hopkins on studies of HIV-1 transmission.

A Fogarty postdoctoral fellow from Peru, at the University of Miami, has immunized HIV-infected infants to determine the effectiveness of Hemophilus influenzae type b vaccine in preventing meningitis. A new ELISA blood test was developed to detect immunity. This study has now been expanded to include other vaccine antigens (diphtheria and tetanus) with the ultimate goal of learning the cause of immunodeficiency in HIV-1 infected children.

B cell lymphoma is a serious complication of patients with AIDS. A Fogarty postdoctoral fellow from Russia, at UCLA, is investigating the role of interleukin 6 in the development and growth of this lymphoma. Early evidence suggests that an overproduction of interleukin 6 may be induced by components of the AIDS virus. If this is the case, it may be possible to devise drugs to reverse the role of interleukin 6 in the occurrence of this AIDS-associated lymphoma.

Mr. Stokes: To what extent are drug trials being supported? How many?

Dr. Schambra: One of the main goals of the training program is to facilitate future international trials of anti-HIV drugs and HIV vaccines. Trainees who are now returning to their home countries are prepared to assist their countries in such trials. Among the 4 drug trials already begun involving FIC trainees are a study of the safety and tolerance of AZT administered to HIV-1 infected children, the use of Dapsone in the prophylaxis of pneumocystis carinii pneumonia and toxoplasmosis and the chemoprophylaxis of TB in HIV-infected individuals.

Mr. Stokes: What regions of the world have been identified as sites for vaccine testing and field trials?

Dr. Schambra: The five countries identified as potential future sites for HIV vaccine testing and field trials by WHO/GPA are Rwanda, Uganda and Côte D'Ivoire in Africa, Brazil and Thailand. The FIC AIDS training programs are actively involved in all of these countries.

Mr. Stokes: To what extent are you working with researchers from Uganda and other African countries where the incidence of AIDS is wiping out generations of people?

Dr. Schambra: The FIC AIDS training programs have been working with researchers from Uganda and other African countries where the impact of HIV/AIDS has been particularly devastating. Through the first 3 years 117 African scientists have participated in the program including 18 from Uganda, 21 from Malawi, 17 from Kenya, 17 from Senegal, 11 from Rwanda and 10 from Zaire.

TUBERCULOSIS

Mr. Stokes: I understand that the Institute is working with other PHS agencies to combat tuberculosis. What type of efforts are you supporting in this area?

Dr. Schambra: The FIC has been working with the Centers for Disease Control, the National Institute of Allergy and Infectious Diseases, the National Heart Lung and Blood Institute, the Food and Drug Administration, the U.S. Agency for International Development, the World Bank, the World Health Organization, and the Union Against Tuberculosis and Lung Disease in organizing the First World Congress on Tuberculosis to be held this November in Bethesda. The Congress will focus on the goal of global tuberculosis control through basic and applied research in the diagnosis, treatment and prevention of tuberculosis as well as behavioral and operational research. Program evaluation, quality assurance, and the epidemiologic, economic and social aspects of tuberculosis will be discussed. Problems of special significance, such as the impact of HIV and drug resistance, will be addressed. In addition, FIC AIDS trainees are involved in a number of research projects related to various aspects of tuberculosis.

Mr. Stokes: What level of resources are being requested for FY 1993?

Dr. Schambra: Since our effort in tuberculosis is primarily the coordination and support of the First World Congress on Tuberculosis which will occur in FY 1992, we have not specifically identified any funds in FY 1993. The FIC will provide $100,000 for the Conference in FY 1992.

HYPERTENSION AND DIABETES

Mr. Stokes: The institute is studying geographic differences in the disparate incidence of hypertension and diabetes among African- American and Caribbean populations. What types of activities are being supported in this area? Are there any findings you can share with the committee?

Dr. Schambra: In FY 1990 the FIC, through its Latin American and Caribbean Initiative (LACI), supported exploratory meetings between NIH scientists and scientists at the University of the West Indies (UWI) and the Commonwealth Caribbean Medical Research Council (CCMRC). Participants agreed that highly qualified researchers, population data banks, and access to populations were available that would provide the opportunities for collaboration on comparative studies of African-American and Caribbean populations in such areas as hypertension, diabetes, lupus, osteoporosis, asthma, cancer, and AIDS.

These findings led to an NIH supported conference on "Research Resources and Opportunities for Collaborative Research in the Caribbean." NIH and UWI scientists who participated identified mutual interests in pursuing joint studies particularly directed to hypertension and diabetes, lupus and osteoporosis in African-American and Caribbean populations.

To date, FIC's initial investment in the exploration of U.S.-Caribbean research interests has resulted in FIC support of scientists at the UWI campus at the Queen Elizabeth Hospital in Barbados and at Loyola University of Chicago to collaborate on a study of the role of glucose intolerance in diabetes mellitus as a corollary of ongoing hypertension research supported by an NHLBI grantee. In addition, the NHLBI has provided supplemental funding to enable Loyola's population-based comparative studies on hypertension and diabetes in blacks in Africa, the United Kingdom and the United States to include the Caribbean; and the NIDDK has also provided funding to the Loyola University of Chicago for comparative diabetes research in African-Americans and the Barbados population.

To communicate these findings to a wider U.S. scientific audience, FIC staff co-authored a paper on "NIH Interests in International Collaborative Research on Ethnicity and Disease" which presented the NIH-Caribbean experience as an effective model for developing cross-national research on hypertension, diabetes and other disease risks among African-American and Caribbean populations.

Mr. Stokes: How many researchers are being supported?

Dr. Schambra: In FY 1991, the FIC supported eight American researchers to participate in the 1991 CCMRC Conference on "Research Resources and Opportunities for Collaborative Research in the Caribbean" in Barbados. We also supported one American and one Jamaican researcher to develop a joint study at the University of West Indies on screening medicinal plans for antiepileptic activity.

Mr. Stokes: Are they Caribbean or American researchers?

Dr. Schambra: Nine American and one Jamaican researchers received LACI support.

Mr. Stokes: What level of funding is being requested for this activity in FY 1993?

Dr. Schambra: Within the FY 1993 President's Budget, we are anticipating about $600,000 to support all scientific areas of collaboration under our Latin American and Caribbean Initiative.

SCHOLARS-IN-RESIDENCE

Mr. Stokes: How many Scholars-in-Residence currently are at the NIH?

Dr. Schambra: Ten Fogarty Scholars are currently in residence at the NIH.

Mr. Stokes: Of this number, how many are from Third World countries?

Dr. Schambra: One of the Scholars is from Brazil.

Mr. Stokes: Are there any this year from Africa?

Dr. Schambra: There are no Scholars from Africa this year. However, in an attempt to increase the participation of Africans in the program, I have written to senior officials of fourteen major African medical schools and research institutes to ask them to identify potential candidates.

I might mention that Dr. A. Olufemi Williams, the first Fogarty Scholar from Africa (Nigeria), has completed a book which he was working on while at FIC. Entitled, "AIDS: An African Perspective," the book characterizes the features of the disease in Africa from clinical, pathological, and epidemiological perspectives.

FUNDING FOR FOREIGN VS. U.S. SCIENTISTS

Mr. Stokes: Last year, we discussed the level of funding supporting foreign nationals and the amount supporting U.S. citizens. You indicated that 41 percent of the budget for international research went to foreign nationals. Only about 2 percent supported American scientists on fellowships abroad. What are the current funding levels?

Dr. Schambra: Data collected for international expenditures for FY 1991 shows a modest increase in the level of funding supporting foreign nationals, from 41 percent to 47 percent, and still about 2 percent for American scientists.

Mr. Stokes: What are you doing to address this situation?

Dr. Schambra: Last year we modified our Senior International Fellowship (SIF) program, the program that supports research activities of American scientists abroad, to provide the opportunity to divide the fellowship into as many as three separate terms within a 3-year period. So rather than going abroad for 9 to 12 months, this allows American scientists some flexibility in making a commitment to work abroad. Because of this flexibility, we do expect increased participation in the SIF program in FY 1993.

We are also exploring two new initiatives with the NIH Office of Minority Health that would provide opportunities for American minority students and researchers to study and work abroad. One is an International Minority Research Scholarship Program which would provide support for undergraduate and predoctoral minority students to study abroad for the summer. The other is a Minority International Research Fellowship Program which would provide support for minority researchers to work in foreign laboratories for one to two years.

Although the data suggest an imbalance in the support of foreign versus American scientists, as mentioned in my earlier testimony the U.S. benefits from this cooperative strategy because science has become more global. Investing in the support of foreign scientists not only strengthens our ties with the foreign countries, but also further enhances our chances of sharing future collaborative research efforts to attack disease outbreaks before they become global emergencies.

AMERICAN MINORITY RESEARCHERS

Mr. Stokes: As raised with Dr. Healy today, it appears that the Management Information Unit at NIH is able to use "IMPAC" data to ascertain the level of minority participation throughout the NIH extramural activities. Last year, you indicated that this type of data was not available. Would you contact this office and ascertain for me to what extent are American minority researchers participating in your programs?

Dr. Schambra: Based on the data available for 1991, 4 of 39 Senior International Fellowships were awarded to American minority researchers.

MINORITY EFFORTS

Mr. Stokes: How many and what percentage of employees of your institute are minorities?

Dr. Schambra: Of total FIC FTEs, 12, or about 17% are minorities.

Mr. Stokes: Please provide a breakdown by race and grade level.

[The information follows:]

STAFFING AS OF DECEMBER 28, 1991

		MINORITIES				
				NATIVE		
	TOTAL	BLACK	HISPANIC	ASIAN	AMERICAN	TOTAL
SES	1					
GS 15	10					
14	9	1				1
13	2					
12	4					
11	3					
10	2					
9	4			1		1
8	2					
7	7	1				1
6	6	1				1
5	13	2	2	1		5
4	7		2			2
Commissioned Officers	2			1		1
	72	5	4	3	0	12

Mr. Stokes: How many are employed in a research capacity?

Dr. Schambra: FIC programs do not include an intramural research component, therefore, we do not employ individuals in a research capacity.

Mr. Stokes: Please describe for the Committee the resources and funding levels which will be provided for minority-specific research activities in FY 1993?

Dr. Schambra: About $7.6 million of FIC's FY 1993 budget will support cooperation with African, Asian, and Latin American scientists to conduct research that would include sickle cell anemia, diabetes, hypertension, viral-caused cancers, tuberculosis and AIDS.

Mr. Stokes: How do these levels compare to last year's levels?

Dr. Schambra: This compares to about $7 million in FY 1992.

Mr. Stokes: Total funding represents what percentage of your budget?

Dr. Schambra: The $7.6 million for FY 1993 represents about 59 percent of the FIC's science budget.

Mr. Stokes: To what extent are you working with the Office of Minority Health to effectuate these goals?

Dr. Schambra: Following discussions on minority issues with the NIH Office of Minority Health, the FIC developed several new initiatives to increase minority participation in the biomedical and behavioral sciences through international programs. These initiatives are under review by the FIC and the NIH Office of Minority Health. In addition to the two new initiatives I mentioned earlier that would provide opportunities for minority students and researchers to study and work abroad, we are also discussing a Minority International Research Grant Program which would provide support to RCMI institutions to develop international collaborative research activities.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

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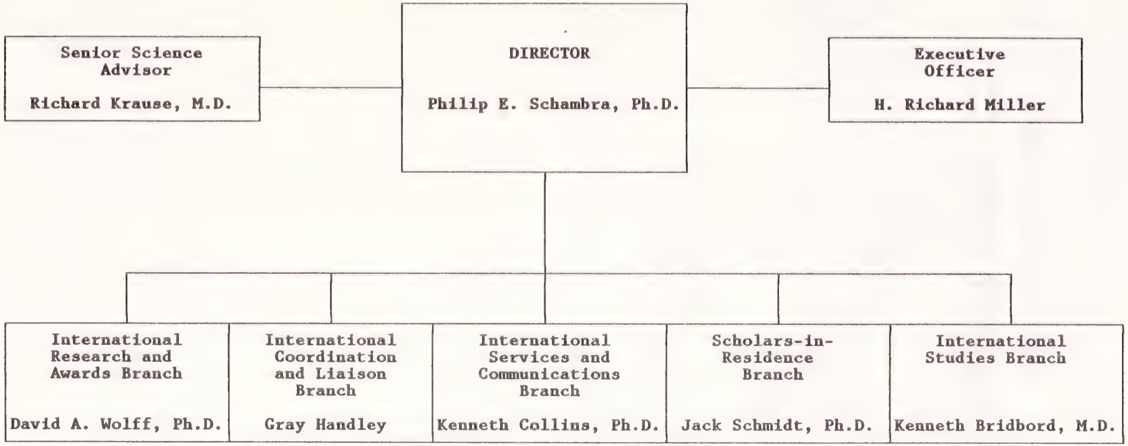
NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center

Organizational Structure


DIRECTOR
Philip E. Schambra, Ph.D.
Senior Science Advisor
Richard Krause, M.D.
Executive Officer
H. Richard Miller
International Research and Awards Branch
David A. Wolff, Ph.D.
International Coordination and Liaison Branch
Gray Handley
International Services and Communications Branch
Kenneth Collins, Ph.D.
Scholars-in-Residence Branch
Jack Schmidt, Ph.D.
International Studies Branch
Kenneth Bridbord, M.D.

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

For carrying out the activities at the John E. Fogarty International Center, [$19,922,000] $20,727,000: Provided, That of the funds made available under this heading, $800,000 shall not become available for obligation until September 30, [1992] 1993.

(Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 1991)

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center for Advanced Study in the Health Sciences

Amounts Available for Obligation 1/

	1991 Actual	1992 Appropriation	1993 Estimate
Appropriation	$18,059,000	$19,922,000	$20,727,000
Section 514(a) reduction..........	-105,000		
Section 514(b) reduction..........	-435,000	---	---
Section 214 reduction.............		-24,000	
Section 513(a) travel reduction...		-250,000	
Section 513 (a) S&E reduction.....		-39,000	
Subtotal, adjusted appropriation	17,519,000	19,609,000	20,727,000
Unobligated balance, lapsing	-14,000	---	---
Total, Obligations ..	17,505,000	19,609,000	20,727,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: FY 1991 - $1,010,000; FY 1992 - $1,750,000; FY 1993 - $2,000,000.

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Budget Mechanism

(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	No.	Amount	No.	Amount	No.	Amount
Research Grants:						
Other Research	213	$10,836	227	$12,133	250	$12,885
	FTEs		FTEs		FTEs	
Research Management and Support	67	6,683	77	7,476	79	7,842
Total	67	17,519	77	19,609	79	20,727

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

CROSSWALK - 1991 Actual

(Dollars in thousands)

	Mechanism		
	Research Grants		
PROGRAM ACTIVITY:	Other Research	Research Management and Support	Total
International research activities ...	$10,836	---	$10,836
Research management and support	---	$6,683	6,683
Total	10,836	6,683	17,519

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

CROSSWALK - 1992 Appropriation

(Dollars in thousands)

	Mechanism		
PROGRAM ACTIVITY:	Research Grants Other Research	Research Management and Support	Total
International research activities	$12,133	---	$12,133
Research management and support	---	$7,476	7,476
Total	12,133	7,476	19,609

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

CROSSWALK - 1993 Estimate

(Dollars in thousands)

	Mechanism		
	Research Grants		
PROGRAM ACTIVITY:	Other Research	Research Management and Support	Total
International research activities	$12,885	---	$12,885
Research management and support	---	$7,842	7,842
Total	12,885	7,842	20,727

John E. Fogarty International Center
for Advanced Study in the Health Sciences

CROSSWALK SUMMARY

(Dollars in thousands)

PROGRAM ACTIVITY:	FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate
GRANTS:			
International Research Fellowships:	$3,955	$4,891	$4,613
Competing/Noncompeting	2,639	2,697	3,109
Stipend Increases	---	600	---
Latin American/East. European Initiative	1,316	1,594	1,504
Senior International Fellowships:	1,079	854	954
Competing/Noncompeting	1,079	614	705
Latin American/East. European Initiative	---	160	249
Scholars-in-Residence Awards:	478	640	618
Competing/Noncompeting	478	470	394
Latin American/East. European Initiative	69	170	224
Fogarty Int'l Res. Collab. Award (EEI/LAI)1/	---	490	1,237
Neurosciences Fellowships (EEI)	172	90	90
Environmental Fellowships (EEI)	---	90	90
Conferences and Workshops	10	---	---
AIDS Training and Research:	5,142	5,078	5,283
Latin America	2,108	2,082	2,166
Africa	1,631	1,611	1,676
Far East/Western Pacific	938	926	963
Eastern Europe/USSR	375	370	385
Other	90	89	93
GRANTS, TOTAL	10,836	12,133	12,885
RESEARCH MANAGEMENT AND SUPPORT:			
FIC Scientific Programs:	1,344	1,639	1,812
Latin American Initiative	227	280	221
Eastern European Initiative	499	560	442
Scientist Exchanges	557	439	439
Conferences & Workshops	61	300	150
Human Frontier Science Program	---	---	500
Japan Summer Institute	---	60	60
Services to NIH Sci. Programs:	1,748	1,870	1,939
Visiting Program	792	844	875
Stone House	172	184	191
International Coordination	711	767	795
Attaches Abroad	73	75	78
Program Management:	3,591	3,967	4,091
OD, OAM, OPPE, IRAB, ISB	2,381	2,590	2,686
Advisory Board/TAPS/Other Operating Costs	1,210	1,377	1,405
RESEARCH MANAGEMENT AND SUPPORT, TOTAL	6,683	7,476	7,842
TOTAL FIC	17,519	19,609	20,727

1/ EEI/LAI=Eastern European Initiative/Latin American Initiative

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NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Summary of Changes

1992 Estimated budget authority	$19,609,000
1993 Estimated budget authority	20,727,000
Net change	+1,118,000

Changes:	1992 Current Estimate Base		Change from Base	
	Pos. (FTEs)	Budget Authority	Pos. (FTEs)	Budget Authority
A. Built-in:				
1. Within grade increase		$3,731,000		+$34,000
2. Annualization of 1992 pay raise		3,731,000		+39,000
3. January 1993 pay raise		3,731,000		+103,000
4. One less day of pay		3,731,000		-13,000
5. Payment for centrally furnished services		868,000		+4,000
6. Service and supply fund increase		308,000		+37,000
7. Increased cost of supplies, materials, and other mandatory program expenses		2,877,000		+158,000
8. DHHS Working Capital Fund increase		68,000		+ 4,000
Subtotal, built-in				+366,000
B. Program:	POS. (FTEs)		POS. (FTEs)	
1. Other research		12,133,000		+752,000
2. Research management and support:	77	1/	+2	1/
Subtotal, program			+2	+752,000
Total changes			+2	+1,118,000

1/ Support for FTE's will be provided by participating agencies.

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Budget Authority by Activity

(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	FTEs	Amount	FTEs	Amount	FTEs	Amount
International Research Activities	--	$10,836	--	$12,133	--	$12,885
Research Management and Support	67	6,669	77	7,476	79	7,842
Subtotal, Obligations ..	67	17,505	77	19,609	79	20,727
Unobligated Balance Lapsing		14		---		---
Total, Budget Authority	67	17,519	77	19,609	79	20,727
HIV/AIDS	(4)	(5,351)	(4)	(5,597)	(4)	(5,849)

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Budget Authority by Object

	1992 Appropriation	1993 Estimate	Increase or Decrease
Total number of full-time permanent positions	74	77	+3
Total compensable work years:			
Full-time equivalent employment	78	80	+2
Full-time equivalent of overtime and holiday hours	1	1	---
Average ES Salary	$104,000	$108,000	+4,000
Average GM/GS grade	9.00	9.00	---
Average GM/GS salary	$36,551	$37,704	+1,153
Average salary, grades established by act of July 1, 1944 (42 USC 207)	$37,515	$42,602	+5,087
Average salary of ungraded positions	---	---	---
Personnel compensation:			
Full-time permanent	$2,476,000	$2,897,000	+421,000
Other than full-time permanent	121,000	142,000	+21,000
Other personnel compensation	104,000	122,000	+18,000
Special personnel service payments	46,000	54,000	+8,000
Total personnel compensation	2,747,000	3,215,000	+468,000
Personnel benefits	601,000	703,000	+102,000
Benefits for former personnel	4,000	4,000	---
Travel and transportation of persons	106,000	112,000	+6,000

	1992 Appropriation	1993 Estimate	Increase or Decrease
Transportation of things	20,000	19,000	-1,000
Rent, communications and utilities ...	185,000	176,000	-9,000
Printing and reproduction	53,000	50,000	-3,000
Other services:			
Centrally furnished services	868,000	872,000	+4,000
Other	2,747,000	2,554,000	-193,000
Supplies amd materials	60,000	57,000	-3,000
Equipment	85,000	80,000	-5,000
Grants, subsidies, and contributions..	12,133,000	12,885,000	+752,000
Total	19,609,000	20,727,000	+1,118,000

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Significant Items in the House and Senate Appropriations Committee Report

Responding to international disease threats

The House, in its report 102-121, page 100, stated "...the Committee has concerns about the mechanisms for a timely response to emerging international disease threats. It was interested to learn that the FIC could use its International AIDS Research and Training Program as a model for future efforts to meet other global research challenges that stem from emerging microbes, global climate change, environmental pollution, and other disease threats."

The Senate, in its report 102-104, page 141, stated "...The Committee was interested to learn that the FIC International AIDS Research and Training program can now be used to rapidly respond to emerging international disease threats, and could serve as a model for future efforts to meet global research challenges that may arise from emerging microbes, global climate change, environmental pollution, and other disease perils."

Action Taken or to be Taken - The FIC recently convened a review group of expert scientists to review the status of progress under its AIDS International Training and Research Program (AITRP) and to make recommendations for the future. One of the questions considered by this group was whether the FIC AIDS training program should gradually expand beyond its initial focus on HIV/AIDS in the future (e.g., STDs, related infectious diseases, emerging microbes, child survival).

The group recognized that the concept and model of the AITRP would be useful in addressing epidemic microbial infections in the world and the methodologies in the AITRP are applicable. The group recommended that HIV/AIDS should remain the focus of the current program and that diseases strongly associated with AIDS (e.g., STDs) should be included within this focus.

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1992 Amount Authorized	1992 Appropriation	1993 Amount Authorized	1993 Budget Request
Research and Investigation	Section 301	42§287b	Indefinite	$19,609,000	Indefinite	$20,727,000
International Cooperation	Section 307	42§287b	Indefinite		Indefinite	
Total Budget Authority				19,609,000		20,727,000

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center for Advanced Study in the Health Sciences

Appropriation History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1984	$9,189,000	$11,584,000	$11,088,000	$11,336,000
1985	11,426,000	11,526,000	11,929,000	11,679,000
1985 Proposed Rescission	(241,000)	---	---	---
1986	11,464,000	11,529,000	11,606,000	11,551,000
1986 Sequester	---	---	---	(497,000)
1987	11,305,000	11,443,000	11,420,000	11,420,000
1988	11,166,000	12,128,000 3/	11,166,000	15,651,000
1989	11,338,000	16,074,000	16,474,000	15,848,000
1990	10,622,000 4/	15,579,000	15,532,000	15,516,000
1991	16,355,000	18,682,000	17,436,000	17,519,000 4/
1992	19,922,000	19,922,000	19,922,000	19,609,000 5/
1993	20,727,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.

2/ Does not include funding for AIDS research. Consolidated at the Secretary's level.

3/ Does not include HIV-related funds, which were requested in a consolidated amount under the Office of the Assistant Secretary for Health.

4/ Reflects enacted administrative reductions of $540,000.

5/ Reflects enacted administrative reductions of $313,000.

Justification

John E. Fogarty International Center for Advanced Study in the Health Sciences

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
67	$17,519,000	77	$19,609,000	79	$20,727,000	+2	+$1,118,000

General Statement

The John E. Fogarty International Center (FIC) for Advanced Study in the Health Sciences, National Institutes of Health (NIH), came into being in part due to a vision of Rep. John E. Fogarty, who in 1963 was quoted as saying, "I would like to see...at Bethesda a great international center for research in biology and medicine dedicated to international cooperation in the interests of the health of mankind." This vision became a reality when the FIC was established in 1968.

Since that time, many changes have taken place, including the globalization of science. It is in this context that the FIC has important new opportunities for leadership in international cooperation in medical research. The mission of the FIC is to improve the health of the people of the United States and other nations through the promotion of international cooperation and advanced study in the biomedical sciences.

To accomplish this mission, FIC's goals are to (1) facilitate the assembly of scientists and others in the biomedical, behavioral, and related fields for discussion, study and research related to the development of health sciences internationally; (2) provide research programs, conferences and seminars to further international cooperation and collaboration in the life sciences; (3) provide postdoctoral fellowships for research training in the United States and abroad, and promote exchanges of senior scientists between the United States and other countries; and (4) coordinate the activities of NIH that are concerned with health sciences internationally.

As the international component of the NIH, FIC advances national and international health research priorities by:

- Providing leadership in identifying and advising on international research opportunities and policy issues;

- o Assembling international experts to examine research opportunities that pertain to new and emerging challenges to health;
- o Enabling U.S. scientists to gain access to innovative foreign research methods and technologies, and study unique populations and environments in other countries through cooperative programs;
- o Contributing to the development of a global health research capacity to identify and prevent regional health problems before they become global emergencies; and
- o Fostering international opportunities to exchange scientific information and resources, and to more efficiently manage research costs and labor through international cooperation.

The challenge of the FIC today is to continue to address the ever expanding health issues that affect the well-being of people around the world. Although many outstanding accomplishments have been achieved in conquering health threats, we are still at risk from many infectious and chronic and disabling diseases. FIC's programs provide hope for diminishing these disease threats through its international scientific research efforts.

The ever-increasing rapid pace and travel patterns of today's populations contribute to the global spread of infectious diseases, and this added risk factor in disease transmission demands increasing cooperative research efforts. The key elements of the FIC programs are exceptionally suited to solving today's health problems. They provide opportunities to increase scientific knowledge in the research community, and to exchange this knowledge with scientists worldwide.

FIC's programs support all of the NIH Strategic Health Goals, while also targeting specific health areas. These areas of emphasis include: reducing disease morbidity and mortality; preventing disease and disability and promoting health; changing behavior to improve health and prevent disease; identifying and combating new disease threats; and meeting the challenge to health from a changing environment.

Program Activities

FIC supports a broad spectrum of biomedical research areas including infectious diseases such as AIDS and tuberculosis; chronic illness such as cardiovascular and neurological diseases, cancer, arthritis and diabetes; and other conditions such as aging, human development, and communicative disorders. Through its distinctive international programs, FIC supports cooperative research and training through its International Research Fellowship Program (IRF), Senior International Fellowship Program (SIF), Scholars-in-Residence Program (SIR), International AIDS Research and Training Program, and Research Collaboration and Development Awards for scientists from two geographic regions--Central and Eastern Europe, and Latin America and the Caribbean.

The FIC administers the NIH Visiting Program for the Institutes, Centers and Divisions of NIH. Through this program, foreign postdoctoral scientists and senior foreign scientists conduct research in the NIH laboratories in collaboration with their American colleagues.

FIC also has a longstanding involvement with managing the NIH Biomedical Research Exchange Programs and the PHS Health Scientist Exchange Programs. These collaborative efforts further contribute to international research collaboration by promoting contacts and cooperation between well-qualified health professionals and biomedical scientists in the U.S. and participating countries.

Enhanced Research Opportunities

By anticipating the research opportunities brought on by the changing circumstances in Europe and elsewhere, the FIC expanded collaborative research opportunities in Central and Eastern Europe, including the Republics of the former Soviet Union, and in Latin America and the Caribbean. These FIC regional initiatives, begun in late 1990, continue to fund research efforts between American biomedical scientists and scientists from these regions.

As an extension of the regional initiatives, but with an emphasis on the neurosciences in support of the congressionally-designated "Decade of the Brain", FIC established the International Neurosciences Fellowship Program in FY 1991 to support mid-career Central and Eastern European scientists to conduct collaborative research in the U.S. Funds for the fellowships are granted by FIC, with research cost supplements provided by NINDS.

Another program that extends research opportunities to regional scientists is the Central and Eastern Europe Fellowship Program in the Environmental Health Sciences. This joint program between the FIC and NIEHS promotes research collaboration between environmental health scientists in these regions and laboratories in the U.S. and is available to foreign scientists who wish to collaborate with NIH intramural and extramural scientists.

FIC has also launched a new program in FY 1992 that will provide small research grants to U.S. biomedical scientists to support their collaboration with counterparts in Central and Eastern Europe, and Latin America and the Caribbean. This new program, the Fogarty International Research Collaboration Award (FIRCA), provides funding so that American and foreign scientists can collaborate in each others' laboratories for limited periods. When needed, the purchase of essential equipment and supplies for the collaborating foreign scientists will further increase opportunities for important research collaboration.

The FIC will continue to provide support for the International Research Fellowship Program and to implement strategies designed to highlight and strengthen program effectiveness in the research arena. Applications for fellowships will now be accepted from the Czech and Slovak Federal Republic, the Russian Republic, the Peoples' Republic of Mongolia, the Philippines and

South Africa. With these additions, applications will now be received from 62 countries. Beginning in FY 1992, the fellowship program will provide the first substantial stipend increase in eight years.

A new fiscal responsibility for the FIC in FY 1993 concerns funding for the Human Frontier Science Program (HFSP). The HFSP supports international cooperation in molecular and cell biology and the neurosciences through the award of research grants, fellowships, and conferences. It is funded primarily by Japan, but is operated in cooperation with the other Economic Summit countries. Following a policy review, the United States has decided to contribute to the HFSP in FY 1993, and the NIH is one of four Federal agencies (NIH, DOE, NSF and NASA) that will support the HFSP activities. The NIH's contribution will be $1,000,000, with $500,000 provided by the FIC and $500,000 provided by those NIH ICDs with specific scientific interest in the program. The FIC will coordinate the NIH contribution to the program.

The FIC will also serve as the coordinating center for the program operations of the International Cooperative Biodiversity Groups (ICBG). The ICBG represents an interagency program involving the National Institutes of Health, the National Science Foundation, and the U.S. Agency for International Development, to promote biodiversity conservation, drug development from natural products, and economic growth in developing countries.

Program Purpose and Method of Operation

The FIC supports extramural research through its international fellowship and awards programs. By providing research opportunities through these programs, research advances can be made in such key areas as molecular medicine, vaccine development, structural biology and biotechnology.

FIC's International Research Fellowships and Senior International Fellowships provide funding for foreign scientists to work in well-equipped research laboratories in the United States and for U.S. scientists to conduct research in advanced laboratories and unique field sites abroad.

The Scholars-in-Residence Program has brought to the NIH many of the world's leading biomedical scientists, including four Nobel Laureates. These distinguished scientists are nominated by leading researchers within the NIH biomedical community and while in residence at the NIH stimulate and enhance the scientific environment of the NIH intramural research program.

FIC's International AIDS Training and Research Program is designed to provide training in epidemiology related to AIDS and in basic and clinical AIDS research, principally for foreign scientists and health professionals from developing countries. Epidemiological research, clinical trials of vaccines and drugs, and the evaluation of various methods of prevention, must be performed in developing countries where the disease is epidemic as well as in the U.S. This requires collaboration between U.S. scientists and the foreign scientists trained by the FIC programs. These training programs are being closely coordinated with AIDS vaccine research and international AIDS research programs supported by the NIAID, the NCI, and the World Health Organization's Global Programme on AIDS (WHO/GPA). Knowledge developed through this effort will be applicable to treatment and prevention programs in the U.S.

FIC's new extramural research program, the Fogarty International Research Collaboration Award (FIRCA), and the expanded regional initiative programs targeting research in neurology and environmental health, all contribute to increased collaborative activity that serves to enhance international research relationships.

FIC's Research Management and Support (RMS) area provides funding for a variety of scientific program activities as well as administrative functions. General management and overall administrative expenses are included in this activity, as well as staff support. However, a significant portion of FIC's RMS funds are devoted to the support of major scientific program activities that include the International Services and Communications Program, the International Research Coordination and Scientist Exchange Programs, AIDS research support activities, and international conferences.

Funding for the Fogarty International Center during the last 5 years has been as follows:

	Amount 1/	FTE
FY 1988	$13,799,000	58
FY 1989	14,018,000	59
FY 1990	15,656,000	59
FY 1991	17,519,000	67
FY 1992	19,609,000	77

1/ Excludes Gorgas Memorial Institute

Overall Budget Policy

The FY 1993 budget request for the FIC is $20,727,000, an increase of $1,118,000 over the comparable FY 1992 level of $19,609,000.

The request includes 79 FTEs, an increase of 2 over the FY 1992 level of 77. The additional FTEs will be used to support the International Cooperative Biodiversity Groups (ICBGS) program. The FIC will serve as the coordinating center for the program and the cost of the FTEs will be supported by the participating agencies.

A total of $12,885,000 is requested in Other Research, reflecting a net increase of $752,000 from the FY 1992 appropriation. The funding will provide for 250 awards for FIC International Fellowships, Fogarty International Research Collaboration Awards, AIDS training grants, and Scholars-in-Residence Fellowships. The increased funding will enable the FIC to fund an additional 23 awards over the estimated number of awards for FY 1992; expand funding support for the Central and Eastern European and Latin American and Caribbean Initiatives, particularly through the newly established extramural FIRCA program, and support for the Senior International Fellowship program. There will be a modest reduction in funding in the International Research Fellowship program.

A total of $7,842,000 will be available in the FIC's Research Management and Support mechanism, reflecting a net increase of $366,000 over FY 1992. The additional funding will be used to support the U.S. contribution to the Human Frontier Science Program and the increased costs of providing services to the NIH science programs, for example, the NIH Visiting Scientists Program and coordination of international activities, as well as for the support of program management activities. To expand the extramural components of recently begun initiatives for Latin America and the Caribbean, and for Central and Eastern Europe, FIC has chosen to reduce the RMS component of these activities.

John E. Fogarty International Center
for Advanced Study in the Health Sciences

International Research Activities

Authorizing Legislation - Section 301 and 307 of the Public Health Service Act. 1993 Authorization: Indefinite.

Budget Authority:

FY 1991 Actual	FY 1992 Appropriation	FY 1993 Estimate	Increase or Decrease
$10,836,000	$12,133,000	$12,885,000	+$752,000

The Senior International Fellowship (SIF) is an FIC award that provides opportunities for U.S. scientists to conduct cooperative research in foreign laboratories. Since 1975, 726 American scientists, supported by SIF awards, have conducted research in 40 countries. Beginning in FY 1991, the SIF award has been modified to increase the foreign living allowance to reflect increased costs in living abroad, and permit awardees to divide the period of support into three terms over a three-year period. In FY 1991, the SIF award supported 39 U.S. scientists who went abroad to continue this international research tradition. For example, a scientist from the University of Massachusetts School of Medicine conducted research in England with an eminent investigator at Cambridge University. The research is concerned with the genes that control the pituitary gland function, the "master" gland at the base of the brain that regulates vital processes such as growth, development and sexual maturation.

Since 1958, FIC's International Research Fellowships (IRF) have been awarded to more than 2,700 scientists from over 50 developing and developed countries. In FY 1991, FIC funded 91 new IRF awards to applicants from 32 countries to conduct collaborative research in U.S. laboratories in 22 states. In addition, in FY 1991, FIC funded second year awards for 50 IRFs who began their fellowships in FY 1990.

For FY 1993, the FIC will continue to fund awards for these programs, as well as the Central and Eastern European neurology and environmental fellowships, to further encourage international research on molecular medicine, neurobiology and biotechnology research and environmental health issues.

The Scholars-in-Residence Program provides funding for eminent scientists to come to the NIH to conduct collaborative research. In addition, scholars participate in lectures, seminars, and other settings which involve interaction with the NIH biomedical research community. Scholars pursue individual research projects and many collaborate with other scientists in NIH laboratories, and organize conferences relevant to their selected research area. During FY 1991, FIC Scholars published 78 scientific papers on a variety of topics, including thyroid hormone function, vitamin A metabolism in health and disease, malaria immunity as related to vaccine development, nerve regeneration, and the clinical and epidemiological features of AIDS in Africa.

During FY 1993, FIC Scholars will conduct studies on: genetic and biochemical determinants of learning and memory; the cause of autoimmune diseases; the development of breast cancer; and the genetic and cellular processes that occur when viruses induce cancer.

The predoctoral and postdoctoral FIC international AIDS training programs are designed to train foreign medical scientists, particularly from those developing countries where the disease is more prevalent. The programs have trained health scientists from more than 50 countries, increasing the number of trained foreign investigators that are needed to strengthen the global research effort on AIDS.

The FIC will continue to support research on AIDS through its research and training programs, through support of focused international workshops on timely issues pertinent to AIDS, and through continuing collaboration with other NIH institutes, CDC, USAID, PAHO and the WHO/GPA. This collaboration is facilitated by the FIC-funded International Network for AIDS Research and Training. Research will include epidemiology in the trainees' home countries to strengthen their efforts in combatting the rapidly growing number of AIDS cases. Relations established between the U.S. and foreign investigators will also lead to long-term mutually beneficial research collaborations and will facilitate drug and vaccine intervention trials as these become feasible.

FIC's new small grants program, the Fogarty International Research Collaboration Award (FIRCA), which began in FY 1992, will continue in FY 1993, with funds awarded to U.S. grantee institutions to support new and expanded research efforts involving collaboration with foreign scientists.

Funding for the International Research Activities Programs during the last 5 years has been as follows:

	Amount
FY 1988	$8,518,000
FY 1989	8,851,000
FY 1990	10,048,000
FY 1991	10,836,000
FY 1992	12,133,000

Rationale for the Budget Request

The FY 1993 budget request for International Research Activities is $12,885,000, which reflects an increase of $752,000 from the FY 1992 appropriation. The increased funding will enable the FIC to fund an additional 23 awards over the estimated number of awards for FY 1992. This will include expansion of the newly established extramural FIRCA Program in support of the Center's two Regional Initiatives and expansion of the Senior International Fellowship Program. There will be a modest reduction in funding for the International Research Fellowship Program.

The following are examples of research projects funded by the International Research Activities Programs.

Molecular Medicine

A strain of transgenic mice was developed by a research fellow from France working at the Salk Institute that will be a model for human diabetes. The work is based on new research in both mice and humans that has implicated specific immunologic characteristics as genetic risk factors for diabetes. These studies may ultimately lead to early intervention and even prevention of diabetes in humans.

Grave's disease is caused by an overactive thyroid gland and can result in cardiac irregularity and disturbances in vision. The search for the abnormalities in the cause of Grave's disease has centered on autoantibodies. Autoantibodies are abnormal immune globulins in the blood that react against substances in the body and result in a disease process. In the case of Grave's disease, one of the autoantibodies is directed against the receptors on the surface of the thyroid cells (to which the thyroid stimulating hormone (TSH) normally attaches), producing a stimulation of the thyroid gland and resulting in hyperactivity. A scientist from Hungary working at the Uniformed Services University of the Health Sciences in Bethesda has shown experimentally that the TSH receptor is a potent antigen and stimulates the production of TSH receptor autoantibodies. Efforts are now underway to prevent the production of the toxic "autoantibodies" in those people who develop Grave's disease. If this can be done, it should be feasible to develop a new and highly successful treatment for Grave's disease.

Research has been conducted by an American research fellow working in Germany to improve the diagnosis and treatment of metachromatic leukodystrophy (MLD), a genetic disease caused by an enzyme disorder. Special methods were developed for diagnostic screening of patients that distinguish between late infantile onset MLD and the adult type. Replacement gene therapy was successful in correcting the enzyme defect in patients' cells grown in the laboratory. This has the potential for eventual treatment for the infantile form of the disease.

Vaccine Development

Vaccines are commonly prepared from inactivated bacteria and viruses (the Salk vaccine), or from harmless attenuated versions of them (the Sabin vaccine). But other strategies are needed to develop new vaccines because these traditional approaches do not always succeed. A Fogarty Scholar from England working at the NIH has developed a novel strategy to develop vaccines. This involves construction of a vaccine from viruses that infect bacteria, but are harmless for humans. These viruses are then modified so that they contain the bacterial substances that stimulate immunity. Vaccines composed of these modified bacterial viruses have been successfully employed in prevention of experimental infections in animals. This work has led to important collaboration with research groups at the NIH who are working on the development of vaccines against AIDS, childhood infections, and tropical diseases such as malaria.

International Health Research

Amebic dysentery continues to be a major public health problem in subtropical and tropical countries as well as a threat to American travellers to those areas. During the past year, a Scholar from Israel, collaborating with scientists at the National Institute of Allergy and Infectious Diseases, identified the special genetic features of the causative parasite, *Entamoeba histolytica*, that are responsible for its virulence. This has led to the development of a diagnostic kit that will have great clinical utility. It will now be possible to identify those patients who are infected with the virulent form and therefore in need of treatment. Research is underway with this new information to develop effective prevention and treatment strategies including vaccines.

Studies at the Medical College of Georgia, by a scientist from Nigeria, have discovered an important relationship between individuals who have sickle cell anemia and also are infected with the malaria parasite. The seriousness of the sickle cell disease is compounded by co-infection with malaria. This double infection results in enlargement of the spleen, leading to diminished immunity to other infectious diseases. Further work is now needed to develop methods for increasing the immunity of patients with sickle cell anemia, including those in the United States.

Cerebral malaria is a fatal form of the disease that is a frequent cause of death in infants and children. This inflammation of the brain is due to red blood cell "clots" in the small blood vessels. A Swedish scientist working at Stanford University has identified the role of the parasite in this "clotting" process. This work should lead to new methods of treatment and prevention of cerebral malaria, particularly in children.

Trypanosomiasis (Chagas disease) is a major chronic parasitic disease in Latin America that can cause heart disease and other internal disorders. Current drugs for treatment are inadequate and progress has been stymied because the parasite has the power to change the molecular components of its outer surface. An unfortunate consequence of this versatility is that the parasite escapes the patient's immune defenses and hampers the development of a vaccine. Scientists from Brazil working at the Seattle Biomedical Research Institute have discovered the mechanisms of gene regulation that govern this rapid turnover of the outer protein overcoat of the parasite. Such fundamental understanding of the biology of the organism opens up a new avenue for drug development.

Neuroscience and Behavior

Disorders of the nervous system have a devastating effect on their victims not only as a result of premature death, but also due to the burden of morbidity on both the individual and society. New advances in neuroscience and behavior have been concerned with the identification of regulatory peptides (small proteins) that influence in a profound way the cognitive behavioral sensory and motor functions of the brain. These peptides are responsible for the transmission of electrical signals among the millions of nerve cells in the brain and between the brain and the other organs of the body. A Scholar-in-Residence at NIH from Sweden has identified the genes that regulate the formation and function of several of these regulatory peptides. He has also identified chemical substances on the cell surface to which the peptide attaches. Peptides influence brain function as a consequence of this attachment process. This sort of research is needed to develop new methods of treatment and prevention of neurological and psychiatric diseases. This research will also be important in understanding the chemical basis of drug addiction and developing prevention strategies.

Rehabilitation Medicine Research

Significant advances have been made in the development of biomaterials that could serve as implants to rehabilitate patients who have physical impairments. A major problem with currently used implant materials has been inadequate adhesion between soft tissues and the biomaterial. This has resulted in limited usefulness of the limb and complications stemming from infections at the implant site. A senior fellow from Tulane University working in Switzerland has developed a reliable method to measure interfacial strength between biomaterials and to observe the factors responsible for adherence. This will lead to the development of new and improved materials by providing quantifiable, experimental systems.

Research on Women's Health

Osteoporosis is a serious chronic disease of bone, particularly in post-menopausal women. In a search for the cause of osteoporosis, new research is concerned with the chemical processes involved in bone formation. One avenue of investigation concerns osteocalcin, a protein involved in bone metabolism. This active bone metabolite may be involved in bone resorption, a process that occurs in osteoporosis. An American senior fellow at Oxford University is studying the structure of osteocalcin using high resolution NMR. Studies on the structure of osteocalin are needed to develop new drugs to reverse its effects and to treat osteoporosis.

AIDS Research

The purpose of the FIC AIDS International Training and Research Program is to train scientists in AIDS epidemiology research as well as appropriate clinical and laboratory investigation. The goal is to increase the number of highly trained epidemiologists, postdoctoral scientists, and clinical investigators, particularly from developing countries where the disease is epidemic, who can collaborate with American scientists on new prevention strategies as well as the conduct of clinical trials of vaccines and drugs.

During the first three years of the program, medical scientists and health personnel from 50 countries, including the U.S., received training. Through FY 1991, 11 U.S. medical schools and schools of public health supported by this program trained nearly 400 investigators from 49 foreign countries. The American faculty conducted over 100 short-term training courses in 20 developing countries, reaching more than 4,500 health care workers and research assistants. During FY 1991, the program continued its expansion to include scientists from Central and Eastern Europe and the Soviet Union.

The following are examples of research conducted through the FIC AIDS programs:

A Fogarty postdoctoral fellow from Zambia, at the University of Miami, in collaboration with a Fogarty fellow from Haiti, has completed an analysis of the safety and tolerance of AZT in a clinical population of children with AIDS. The hypothesis was that AZT can be safely administered to community-based pediatric patients with a minimum amount of clinical and laboratory follow-up to monitor toxicity. Preliminary analysis indicates that the frequency of clinical adverse effects possibly related to AZT in this population was no greater than the frequency of these events noted in the Phase II Pediatric ACTG trial of AZT. One fellow is also playing a key role in compiling data for the International Registry of HIV-1 Exposed Twins in collaboration with scientists from the National Cancer Institute. The fellow from Haiti, upon return to his country, is collaborating with colleagues from Johns Hopkins on studies of HIV-1 transmission.

A Fogarty postdoctoral fellow from Peru, at the University of Miami, has immunized HIV-infected infants to determine the effectiveness of Hemophilus influenzae type b vaccine in preventing meningitis. A new ELISA blood test was developed to detect immunity. This study has now been expanded to include other vaccine antigens (diphtheria and tetanus) with the ultimate goal of learning the cause of immunodeficiency in HIV-1 infected children.

B cell lymphoma is a serious complication of patients with AIDS. A Fogarty postdoctoral fellow from Russia, at UCLA, is investigating the role of interleukin 6 in the development and growth of this lymphoma. Early evidence suggests that an over-production of interleukin 6 may be induced by components of the AIDS virus. If this is the case it may be possible to devise drugs to reverse the role of interleukin 6 in the occurrence of this AIDS-associated lymphoma.

One of the concerns in regard to the diagnosis and prevention of AIDS is the development of a cost effective and easily performed blood test for use in field studies in the developing countries of South America, Africa and Asia. Using recombinant DNA techniques, the envelope protein components of the HIV-1 and HIV-2 AIDS viruses have been produced and employed in a simplified blood test system for detection of the antibodies to the virus. The presence of antibodies is indicative of infection with the AIDS virus. The new test can be performed in one hour at a cost of less than 50 cents per sample. This compares to the current test which requires two days at a cost of nearly $100.00 per sample. This simplified and less expensive test is now being employed in the field by a Fogarty fellow from Senegal, working at Harvard, to determine its reliability. Pregnant women are enrolled in the study at delivery, and the test will be used to determine transmission of AIDS from infected mother to the newborn. If the test proves successful, it may lead to less expensive testing in the United States.

Foreign scientists who have been trained in U.S. universities are now returning to their home country and setting up research and AIDS control programs. For example, a Fogarty trainee from Honduras returned home to coordinate nationwide AIDS efforts including implementation of sentinel serosurveillance among subpopulations at high risk for HIV-1 infection in STD clinics, among female sex workers, and among adolescents. This is an important first step in control. Another trainee from Honduras has returned home to direct the clinical management of all AIDS cases in the city of Tegucigalpa and to develop a clinical trial with Dapsone for the prevention of Pneumocystis pneumonia and toxoplasmosis in HIV/AIDS patients. A trainee from Haiti is studying the interaction between HIV and tuberculosis and sexually transmitted diseases including possible gene products which may protect against TB infection.

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Research Management and Support

Authorizing Legislation - Section 301 and 307 of the Public Health Service Act. 1993 Authorization: Indefinite.

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
67	$6,683,000	77	$7,476,000	79	$7,842,000	+2	+$366,000

Several major components of FIC research and program activity are funded through the Research Management and Support mechanism structure, providing support for the International Services and Communications Program, the International Research Coordination and Scientist Exchange Program, AIDS research support endeavors, and scientific conferences and workshops. FIC RMS funds also support the administrative requirements of the Center, including staff support and normal program operations costs.

Funding for the Research Management and Support Activities during the last 5 years has been as follows:

	Amount	FTE
FY 1988	$5,281,000	58
FY 1989	5,167,000	59
FY 1990	5,468,000	59
FY 1991	6,683,000	67
FY 1992	7,476,000	77

Rationale for the Budget Request

The FY 1993 budget request for RMS is $7,842,000, providing a net increase of $366,000 over the FY 1992 appropriation. Core program activities are covered in the RMS section along with administrative and program operations costs. Funds are also included for the U.S. contribution to the Human Frontier Science Program. The following examples are illustrative of some of the FY 1992 activities, with plans for similar or enhanced FY 1993 activities, financed from RMS funds.

FIC took the lead role in establishing and sponsoring the International Network for AIDS Research and Training that links together representatives from the FIC, the NIH Office of AIDS Research, the National Institute of

Allergy and Infectious Diseases, the National Cancer Institute, the Centers for Disease Control, the U.S. Agency for International Development, the WHO Global Programme on AIDS, PAHO, and the principal investigators of the 12 FIC AIDS training programs. The network facilitates the coordination of research training needs and the formation of collective strategies to respond to emerging and unanticipated events as the AIDS epidemic progresses. Cooperation through the network also minimizes duplication of effort, not only between the FIC and other NIH grantees, but also between U.S. and other governmental and international organizations. The network's most recent meeting was hosted by FIC on October 9. The agenda constituted the second phase of a major review of the FIC AIDS training programs including possible modifications and enhancements to make the program even more effective during its second five-year cycle beginning in FY 1993.

The FIC collaborated with the Centers for Disease Control and the WHO Global Programme on AIDS in supporting the Second International Course in Surveillance and Applied Epidemiology for HIV and AIDS conducted for public health and medical officials from developing countries. The FIC also contributed partial support in collaboration with NIAID for the National Conference on Women and HIV Infection, for conferences dealing with antivirals and mucosal immunity, and other special international conferences on AIDS including the V and VI International Conferences on AIDS in Africa, held in Zaire and Senegal, respectively.

Because of its major role on behalf of the NIH international AIDS effort, the FIC has continued to provide principal staff support to the World AIDS Foundation in collaboration with staff from the Institute Pasteur in Paris. This collaboration has, to date, resulted in the funding of 36 research projects to assist with AIDS control in developing countries.

FIC also contributed to the Conference on Emerging Microbes and Microbial Diseases, where scientists discussed the changes in bacteria, parasites, and vectors related to changes in human activities that are the cause of important new diseases or the re-emergence of old ones; and a workshop on Drug Development, Biodiversity, and Economic Growth, where participants representing 7 countries, private industry, environmental organizations, and indigenous peoples, discussed how to facilitate the development of pharmaceuticals derived from bioactive natural products while protecting the interests of developing nations that possess such products.

Scientists from 8 countries attended a conference on Cell Volume Regulation organized by a Fogarty Scholar to examine the regulation of cell volume which plays an important role in diverse biological processes, including immune and inflammatory responses, diabetes and other metabolic diseases, ocular diseases and the survival of transplanted organs.

The International Services and Communications Program provides overall administrative and technical support to programs under which foreign scientists come to the NIH to conduct collaborative research with NIH intramural scientists. During FY 1991, FIC arranged for the participation of over 2,750 foreign scientists in laboratories of NIH institutes and other PHS agencies located on the NIH campus. Foreign scientists constituted approximately one-third of the total number of researchers in the NIH intramural community and were major contributors to the scientific publications resulting from the NIH research effort. FIC provides visa, immigration, and other administrative support and advice for the foreign scientists. An important aspect of this work is the analysis and evaluation of new immigration laws and changing immigration policies and regulations and their effects on the NIH Visiting Scientists Program.

The International Research Coordination and Scientist Exchange Program links the international scientific efforts of the NIH with those of other countries of the world. Such linkages have never been more important. The global pattern of diseases threatening human well-being continually changes. FIC's programs weave tightly together to form a comprehensive yet flexible response to those health challenges. During FY 1991, these programs increased the number of collaborating scientists worldwide, and enabled newfound discoveries to be discussed and studies to be undertaken in laboratories in remote areas of the world. Through continuing such combined and collaborative efforts the nature of these diseases can be understood and their incidence reduced.

To accomplish its mission, this program provides policy guidance and direction; assists in the development and management of bilateral and multilateral agreements, programs and initiatives; and analyzes international health and biomedical issues to support NIH, Departmental, and Administration decision makers. It also links the NIH with other international components of the Department of Health and Human Services, the National Science Foundation, the Department of State, the White House Office of Science and Technology Policy, other U. S. government technical agencies, foreign scientific institutions, multilateral organizations and non-governmental bodies concerned with international health and biomedical research. Within this area of activity, during FY 1991 FIC also supported NIH and PHS participation in high level U.S. Government international science and technology policy forums. FIC currently administers NIH participation in 73 formal agreements with 39 countries.

Among these agreements are scientist exchange programs with Austria, Bulgaria, France, Hungary, Poland, Romania, the former USSR, and Yugoslavia. These programs, administered by the FIC, provide unusual opportunities to U.S. and foreign scientists for short-term research collaborations that can lead to more extensive, long-term joint research activities. During FY 1991, under the exchange programs with these eight countries, 20 U.S. scientists conducted research in laboratories of these countries and 34 scientists from these countries conducted research in U.S. laboratories. Under the exchange programs with Austria and France, research collaborations have focused on such areas as Kaposi's sarcoma, molecular biology, hematology, biochemistry, and collaboration on the Klosterneuberger Stroke databank in Austria. Under the Central and Eastern European programs, activities included research and research training in multi-organ transplants, cardiothoracic surgery, neuroradiology, congenital scoliosis, reconstructive surgery, biomechanics, behavioral prevention and control of HIV infections.

The FIC, in collaboration with the PHS Office of International Health and the National Institute of Allergy and Infectious Diseases, administers a bilateral program with India which advances cooperation between American and Indian clinicians, epidemiologists, and biomedical researchers. The program supports basic and developmental research on vaccines for commonly encountered infectious diseases such as bacterial and viral diarrhea, typhoid, acute respiratory infections, tuberculoses, and canine rabies. This has proven to be an effective collaboration which utilizes PHS and USAID funding.

Regional Initiatives

In response to Congressional and scientific interests to expand health sciences research collaboration in new democracies, FIC launched two regional initiatives in FY 1990 to facilitate new and expanded cooperation between NIH scientists and scientists in Central and Eastern Europe, and Latin America and the Caribbean.

On the basis of this first year's experience, FIC expanded FY 1991 regional initiative activities to support both NIH scientists and extramural scientists with active NIH grants. Projects have been funded to enable foreign scientists from these regions to: 1) conduct research and receive training in advanced research methods at NIH laboratories and those of NIH grantees at U.S. universities; 2) make short-term visits to NIH and U.S. universities to develop or conduct research studies; 3) acquire essential research equipment, supplies, material and technical information to strengthen their capacity to conduct research; and 4) conduct research development workshops to exchange data and develop new collaborations.

Central and Eastern European Initiative

In FY 1991, FIC funded 51 research and workshop proposals for joint activities with scientists from seven countries of Central and Eastern Europe: Bulgaria, the Czech and Slovak Federal Republic, Hungary, Poland, Romania, the USSR, and Yugoslavia. Activities were supported with all seven countries; 15 NIH Institutes, Centers or Divisions were involved. Many projects received additional funding from the sponsoring Institute. Scientific workshops related to adolescent health and slow virus zoonoses were held in the Czech and Slovak Federal Republic and funds were provided for what it is hoped will be the first of several workshops in the region on the neurosciences during the Decade of the Brain to provide young scientists with the opportunity to establish international collaborative efforts.

Latin American and Caribbean Initiative

During FY 1991, FIC funded 34 research proposals for the development of new and expanded collaboration with scientists in the Latin American and Caribbean region. Cooperative projects were supported in twelve institutes at NIH and at twelve U.S. universities. Scientists from 9 countries in the region were supported through these awards. Brazil was involved in sixteen of the funded projects, attesting to long-standing interest in U.S.-Brazil collaboration. Mutual priorities and opportunities were also evident in awards involving Chile (4 projects), Argentina (3 projects), and Venezuela and Mexico (2 projects each). Colombia and Costa Rica were each included in projects to increase research skills and to strengthen research infrastructures. In addition, six awards supported multi-country participation in workshops to develop new research studies and apply advanced research methods.

FIC regional initiative funding included support for the following research activities:

Neurosciences

A Russian scientist was supported to collaborate with an NINDS scientist on the effects of transplantation of fetal neurons into the spinal cord of the rat. The results of this study will be applied to spinal cord injury.

A scientist from UCLA received support from FIC to expand collaboration with Brazilian colleagues for research on the physiology and chemistry of chronic brain seizures.

FIC support enabled an NINDS scientist to collaborate with scientists in Barbados to screen compounds isolated from plants for possible medicinal value as a new anti-epileptic drug.

Endocrinology

A Byelorussian scientist was supported by FIC to collaborate with an NIDDK scientist on a newly discovered serum protein in the blood that transports thyroid hormone from the thyroid gland to body tissues. This work is important to understanding diseases such as hyperthyroidism.

FIC support enabled a Hungarian scientist to collaborate with an NICHD scientist to conduct biochemical studies on the adrenal gland and Addison's disease.

Scientists from Barbados and Loyola University received FIC support to collaborate on the study of hypertension and diabetes risk factors among black populations in Africa and the Caribbean.

Growth and Development

FIC support enabled two senior Russian scientists to collaborate with NICHD scientists to study the genetic and molecular regulation of growth and development of Drosophila, research that bears on the cause of birth defects in humans.

A Russian scientist received FIC support to collaborate with a scientist at Roswell Park Memorial Institute on the genetic regulation of alpha-globin genes. The goal is to understand normal cell division in growth and development; and, in cancer, uncontrolled cell division.

Genetics and Molecular Biology

FIC support enabled Hungarian and Czechoslovak scientists to collaborate with NICHD scientists to improve separation methods in DNA electrophoresis, research that is relevant to the human genome project.

A Brazilian scientist received FIC support to work with an NIDR scientist to develop models for targeting expression of genes in cartilage and cartilaginous tissues in vivo.

Biophysics and Cell Biology

FIC support enabled Russian scientists from Moscow and Novosibirsk to collaborate with investigators at NICHD and NIDDK on the chemical processes that occur when influenza viruses infect cells. Such research is needed to develop better vaccines and drugs for influenza.

Bulgarian scientists received FIC support to collaborate with scientists from New Jersey and New York to determine the chemical basis of pulmonary pathophysiology in lung disease in the premature infant.

Environmental Health

Columbia University scientists received FIC support for what is expected to be the first phase of an effort involving NIEHS and four other institutions to bring the most advanced techniques in molecular epidemiology to a study in Poland measuring the effects of air pollution on women and the developing fetus.

FIC support enabled scientists in Poland to collaborate with NCI and NIA scientists on the etiology, early detection, and treatment of cancer, and to study the influence of aging on cancer patient management.

International Health Research

FIC support enabled scientists from Costa Rica and Mt. Sinai Medical School to collaborate on a study of congenital malformations associated with pesticide exposure in Costa Rica.

A scientist at Yale University received FIC support to establish collaborative research with a Brazilian scientist on development of a vaccine against leishmaniasis employing a non-human primate model system.

Strengthening International Research Relationships

FIC has long been committed to improving and enhancing research relationships between the U.S. and other countries. During the past fiscal year, the FIC was involved in the renewal of several successful agreements and the establishment of new bonds with scientists in several foreign countries.

Following are some examples of these agreement activities:

Under the U.S.-USSR Basic Sciences Agreement, FIC organized the visit of a delegation from the USSR Academy of Sciences to NIH in January 1991 to explore the prospects for cooperation in basic biomedical research between NIH and the Academy. The Director, FIC, participated in the U.S.-USSR Basic Sciences Joint Commission Meeting in Moscow in May 1991, where further discussions were held with Academy officials. Mutual interests were identified in the priority areas of cancer, immunology and AIDS, molecular biology and genetics, neurobiology, and clinical research.

Under the U.S.-Japan Science and Technology Agreement, the Director, FIC, was appointed Life Sciences Liaison for the U.S. side and participated in the Joint Working Level and Joint High Level Committee meetings, both of which were held in Japan in 1991. Cooperation is being developed in three new areas involving NIH--bioprocessing, alternatives to laboratory animal use, and human genome research. In addition, five new projects will be implemented between Japanese and U.S. extramural investigators.

Due to discussions held between the Minister of Health of Mongolia and the Director, FIC, the Minister visited NIH in April 1991 to explore the potential for cooperation. Mutual interests were identified in a number of areas and cooperation will begin initially on research related to hepatitis and influenza, involving the National Institute of Allergy and Infectious Diseases.

In March 1991, FIC, the National Cancer Institute, the National Science Foundation, and the U.S. Agency for International Development co-sponsored an international workshop, "Drug Development, Biological Diversity, and Economic Growth." The success of the workshop provided the impetus to design a joint international research program that links drug development from natural products to conservation of natural resources in the countries in which they are found. NIH, NSF, and USAID will pool resources to launch a $1.5 million program beginning in FY 1993, which will be administered by FIC.

FIC participated in the successful initiation of a U.S.-Egyptian program of cooperative research in biomedicine between the Ministry of Health and the Public Health Service. The program is funded by USAID for approximately $5 million over three years and will provide U.S. scientists with unique opportunities in such important public health priority areas as vector-bone diseases, cancer, hypertension, rheumatic heart fever, and genetically-based diseases. Nine projects are based at the NIH, for which FIC is the overall management coordinator.

FIC served as a co-sponsor of the Regional Environmental Center for Central and Eastern Europe's first major conference on environmental health in Budapest in February, 1991. The conference focused on the scientific foundations of risk and health assessment for scientists and policy makers. Environmental health problems in the region were identified and a strategy for the Center's work in response to regional needs outlined.

FY 1992 was the first full year of operation for the U.S.-Hungary S&T Program and remarkable progress was made in implementing the program. FIC directed reviews, ranked proposals, and met with counterparts of the cooperating countries to reach agreement on the proposals funded and maintained general management oversight of the grant awards. Many high quality proposals were received and projects were approved for funding by the U.S. and Hungary at the annual meeting in March and the intercessional meeting in October, which included projects of interest to several NIH institutes.

FIC staff were also involved in the negotiations that led to another S&T agreement. An umbrella S&T agreement was signed in October, 1991, between the U.S. Government and the Czech and Slovak Federal Republic (CSFR). Commitments were made for the U.S. Government and the CSFR to contribute $600,000 each for joint fund activities, where portions of the allocations are for health-related research. The U.S. contribution came from State Department funds.

FIC staff participated in the identification of areas for potential collaboration under the renewal of the U.S.-Venezuela S&T Agreement in Caracas. Natural products development as sources of therapeutic agents was identified as a mutual interest.

International Science Policy Coordination

The FIC Director continued to serve as Vice Chairman of the Federal Coordinating Committee on Science, Engineering, and Technology (FCCSET) Committee on International Science, Engineering and Technology (CISET) and Chairman of the Subcommittee on Science and Technology cooperation with Industrialized countries. These bodies provide government-wide policy guidance on international S&T issues and serve as mechanisms for interagency planning and coordination.

As a result of its CISET role, FIC staff represented NIH on an E.C. forum on drug research and development which resulted in an E.C.-wide White Paper to the European Parliament. FIC provided input on NIH research and policy initiatives and innovative funding models to assist European health research officials in their strategic planning related to drug and vaccine development.

FIC also worked in consultation with other NIH institutes, the Department of State and foreign ministries of other countries to advance U.S. objectives and NIH procedures in connection with ensuring appropriate review of international activities in which human research subjects are involved.

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center for Advanced Study in the Health Sciences

Detail of Permanent Positions

	1991 Actual	1992 Appropriation	1993 Estimate
ES-4	1	1	2
GM/GS-15	10	12	12
GM/GS-14	9	9	9
GM/GS-13	2	4	5
GS-12	4	5	5
GS-11	3	3	3
GS-10	0	1	1
GS-9	4	5	5
GS-8	1	1	1
GS-7	6	7	7
GS-6	6	8	9
GS-5	10	11	11
GS-4	4	4	4
Subtotal	60	71	74
Grades established by the Act of July 1, 1944 (41 U.S.C. 207):			
Director Grade	3	3	3
Total permanent positions ..	63	74	77

AMOUNTS BUDGETED FOR INCREASES IN FULL-TIME EQUIVALENTS

ACTIVITY/POSITIONS	GRADE	NO. OF POS.	O.C. 11 ANNUAL SALARY	O.C. 12 BENEFITS @ 23.0%	O.C. 21 TRAVEL	O.C. 23.1, 23. RENT	O.C. 25 OTHER SERVICE	O.C. 31 EQUIPT.	OTHER OBJECTS	SUB.TOT. NEW COSTS	SUPPORT STAFF SHARE	NO. OF FTE	TOTAL NEW COSTS
FIC Research Management and Support													
International Health Program Office	GS-13	1	$46,210	$10,628	$2,000			$1,000	$1,000	$60,838		1	$60,838
Program Assistant	GS-6	1	19,713	4,534						24,247		1	24,247
			65,923	15,162	2,000			1,000	1,000	85,085		2	85,085 1/

1/ The additional FTEs will be used to support the International Cooperative Biodiversity Groups program. The FIC will serve as the coordinating center for the program and the cost of the FTEs will be supported by the participating agencies.

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center for Advanced Study in the health Sciences

New Positions Requested

	Grade	Number	Annual Salary
Research Management and Support			
International Health Program Officer..............	13	1	$46,210
Program Assistant..............	6	1	19,713
		2	65,923

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Advisory and Assistance Services

For FY 1993, the Advisory and Assistance Services (AAS) budget will be $85,000, an increase of $24,000 over the FY 1992 amount, and will provide for additional costs associated with the Center's review of on-going and re-competing awards programs.

The AAS funds will cover an assortment of activities including costs associated with the expenses for scientific experts and consultants, as well as costs affiliated with the FIC Advisory Board, which will continue to carry out its directive in advising the FIC on effective program execution and collaborating and advising on long-range program plans.

The FIC will continue to obtain the most professional and qualified services in order to maintain the effective management of all FIC program plans and goals. All procurement requests must be approved by the FIC Administrative and Executive Officers to ensure accurate and proper execution of any consultant services request. The qualifications and appropriateness of both the consultant and the service are thus determined only by action of the Center's senior management officials.

Thursday, March 26, 1992.

OFFICE OF THE DIRECTOR

WITNESSES

DR. BERNADINE P. HEALY, DIRECTOR, NIH

JOHN D. MAHONEY, ASSOCIATE DIRECTOR FOR ADMINISTRATION

DR. JOHN W. DIGGS, DEPUTY DIRECTOR FOR EXTRAMURAL RESEARCH, NIH

DR. JAY MOSKOWITZ, ASSOCIATE DIRECTOR FOR SCIENCE POLICY AND LEGISLATION, NIH

DR. VIVIAN W. PINN, DIRECTOR OF RESEARCH ON WOMEN'S HEALTH, NIH

DR. JOHN RUFFIN, ASSOCIATE DIRECTOR FOR MINORITY PROGRAMS, NIH

DENNIS P. WILLIAMS, DEPUTY ASSISTANT SECRETARY, BUDGET, DHHS

INTRODUCTION OF WITNESSES

Mr. Natcher. We take up next the Office of the Director, Buildings and Facilities. We have before the Committee, Dr. Healy, the Director.

Dr. Healy, it is a pleasure to have you back before the Committee and also to have had you each day as we have gone along with the hearings on the NIH requests. As I have said to you, the hearings have been excellent, Dr. Healy, and mainly because of you. I say that to you frankly. We are delighted to have you.

Doctor, before you give us your statement, tell us who you have at the table with you. Nearly all of them are in a nice picture hanging on the wall.

Dr. Healy. Thank you, Chairman Natcher. We do appreciate those pictures.

We have Dr. John Ruffin, Associate Director for Minority Programs; Dr. John Diggs, Deputy Director for Extramural Research; and Mr. John Mahoney, Associate Director for Administration. Starting on my right, Dr. Jay Moskowitz, Associate Director for Science Policy and Legislation; Dr. Vivian Pinn, Director of Research on Women's Health; and, last, but never least, Mr. Dennis Williams, Deputy Assistant Secretary for Budget, DHHS.

Mr. Natcher. Thank you. We will be pleased to hear from you.

Opening Statement

Dr. Healy. Mr. Natcher and Members of the Committee, over the past year activities in the Office of the Director of the National Institutes of Health have been animated by a spirit of striving and commitment. This spirit has resulted in tangible achievements and innovative programs.

As you know from my earlier testimony and that of my colleagues, the NIH is changing, and the Office of the Director has been a catalyst for much of that change. In the process, the Office of the Director itself has been transformed.

Before I describe in detail the ways in which the Office of the Director has changed over the past year—and the achievements that have resulted from our striving and commitment—let me remind you that a Nobel laureate once observed that, "A permanent state of transition is man's most noble condition."

While it may be noble for an individual to exist in a permanent state of transition, I am aware of the fact that it is not necessarily conducive to sustaining the long-term efforts of a large, $9,000,000,000 enterprise.

Each of the administrative and programmatic changes that I have initiated as Director of the NIH is aimed at improving already existing structures and putting into place new mechanisms to enhance NIH's capacity to fulfill its mission: science in the pursuit of knowledge to extend healthy life and reduce the burdens of illness and disability.

Mr. Chairman, the NIH as a whole has always worked at the frontiers, building the foundation of knowledge that ultimately leads to improvements in human health and well-being. To achieve the goals of the mission, we have learned to plan for what lies beyond the horizon.

Over the past year, the NIH has assumed responsibility for such planning—planning not only to capitalize on the extraordinary opportunities in burgeoning areas of biology and medicine but to achieve predictability and stability in the biomedical research community.

STRATEGIC PLAN

The Office of the Director has led a strategic planning process for NIH that builds on past accomplishments, organizational strengths and mechanisms and approaches of proven value and directs a course for our efforts that will prepare for, accommodate and shape our future.

Our strategy for NIH pledges us and the extramural community, as partners, to address opportunities, challenges and needs of a future of intellectual vigor, dedication and integrity. We have already made great strides in creating a corporate sense of common mission and goals, articulating the vital areas of science and policy which the whole of NIH must address, along with the disease-oriented targets of individual institutes.

During the strategic planning process, it became clear that greater emphasis was required in certain areas of the management of NIH. We have identified within the Office of the Director key management positions which reflect those policy priorities.

Consequently, I have recommended to the Secretary the elevation of both the Office of Science Policy and Legislation and the Office of Administrative Management to the level of Deputy Directorates. Each of these offices has made and continues to make significant contributions, not only in the identification of inherent gaps and weaknesses in NIH policy and management but also in the development of the structures and functions to resolve those weaknesses.

In addition, we have established an ethics function on the NIH campus and have instituted new guidelines and are developing new automated procedures for approving outside work requests for NIH scientists to ensure that such activities are carried out in accordance with government ethics rules.

Additionally, the standing of our Division of Equal Opportunity has been elevated to the Office of Equal Opportunity, in order to more effectively act on employees' complaints and interests.

Moreover, we have brought together experts in the areas of legal affairs and communications, both enhancing our ability to accelerate the resolution of issues and to disseminate our research accomplishments more rapidly to our scientific constituency and the public.

The OD has, in addition, assumed a key role in the Department of Health and Human Services' working group on the costs of research. NIH has taken the lead in constructing a data base on allocated overhead associated with research. We are analyzing those data and proposing viable alternatives to improve the system of Federal reimbursement for allocated overhead. This work has laid the foundation for much of the policy analysis that will be taking place at the Office of Management and Budget and the Office of Science and Technology Policy.

Those proposed Deputy Directorates will complement those of the existing Deputy Directors for Extramural and Intramural Research, which have been instrumental in implementing many of the cost management reforms proposed by this committee. We must secure the maximum return on the public investment in our enterprise. This means maintaining a diversified basic and clinical research portfolio managed by the individual institutes, with emphasis on investigator-initiated research and quality management systems.

The OD commitment to the stewardship of public funds demands integrity and fairness in the conduct of our business. For example, the Office of Extramural Programs has provided effective leadership in the area of peer review. With leadership from the institutes, we are reevaluating the role of the study sections to possibly include their review of total costs, as well as quality of science.

Leadership of the intramural research program has been instrumental in defining the facilities and support requirements of the NIH for the next 20 years.

NIH CLINICAL CENTER COMPLEX

The proposed NIH Clinical Center Complex replacement facility will be the most critical component to the vitality of the NIH intramural research program. Also contributing to the continued success of the NIH intramural and administrative components is the Silvio O. Conte Building, which will open this November, housing part of our Child Health and Neurosciences Programs, and the William H. Natcher Building, which will be the gateway to NIH.

STRATEGIC PLAN

This NIH OD organization is the core of my NIH management leadership. Together with the entire OD senior staff and the Directors and senior staff of the institutes, they foster the teamwork necessary for pursuing our national goals within our framework for the strategic plan.

We have increased our efforts to promote better communication among those staff members through regular staff meetings and by the creation of the Executive Council. This Council, composed of OD senior staff and select ICD Directors, will meet on a regular basis to discuss issues of administrative and scientific concern, facilitating a quicker resolution of those problems requiring the input of policy-makers and scientists alike.

As an administrator and manager, I have recognized the value of addressing strategic policy issues of management that undergird our science accomplishments. As a physician, I am also deeply compelled to pursue those programs which promote the public trust.

PROMOTION OF PUBLIC TRUST

Many of the challenges I face as Director of the NIH arise from the interface of current biomedical research and the expectations of our society. The rapid progress and growing complexity of science and the public's heightened expectations for the research enterprise necessitates closer attention to social, legal and ethical issues inherent in biomedical and behavioral research; to professional standards of science; to efficient communication of facts to the public; to the impact of research on health care; and to transferring technology and fostering collaborative endeavors in the public interest.

The advances of research in human genetics, for example, have caused us to reexamine concerns about privacy, potential job discrimination, insurability, and the necessity for counseling those with real or potential genetic diseases. I have begun to address such issues by establishing an issues forum on ethical, legal and social issues, composed of NIH senior staff. The role of this addition will be to coordinate in-depth analysis of the complex array of ethical, legal, social and economic issues arising from biomedical research. The forum will interact with others within the institutes and scientific community in anticipating and addressing the related aspects of these issues.

The creation of such a forum underscores my commitment to ensure that NIH is responsive to the evaluation of these complex issues and public concerns. We must continually earn the public's respect, trust and confidence as we carry out our mission.

Another manifestation of our commitment to the public trust is our pursuit of the inclusion of those who may have been bypassed in many of our past efforts in biomedical research. For the coming fiscal year, I have requested $44,500,000 to continue the Women's Health Initiative. We expect to award contracts to 15 health research centers by the end of the current fiscal year.

MINORITY HEALTH INITIATIVE

I have also requested $45,000,000 to support the Minority Health Initiative, MHI, which is part of an overall increase of 62.8 percent for trans-NIH minority programs.

These funds will be used to coordinate NIH-wide goals and policies aimed at research, training and career development for members of America's minorities. They will also target the improvement of the health status of all minorities across their life span and the expansion of the participation of minorities in biomedical research careers. A wide range of health and behavior problems affecting infant, adolescent, young adult and older minority populations will be assessed.

To expand minority participation in health research endeavors, the initiative will also focus on development, recruitment and retention of minorities in a wide array of research and health services delivery careers.

DIRECTOR'S DISCRETIONARY FUND AND ONE-PERCENT TRANSFER AUTHORITY

These two very important initiatives would not have been possible without the two new authorities of the Director—the Director's Discretionary Fund and the One-Percent Transfer Authority.

Such authorities have also made possible the Shannon Awards. The awards have supported investigators who are pursuing innovative research but have just missed funding through NIH's regular grant mechanisms. Shannon Awards went to more than 310 scientists at 145 research institutions across the country. I plan to continue the Shannon Awards for the coming fiscal year.

In addition, the Director's Discretionary Fund and One-Percent Transfer Authority also allowed us to initiate programs in medical rehabilitation research and science education. Our Office of Science Education, for example, established a life sciences education program that brought elementary and middle-school students to the NIH campus to meet with our scientists and to gain hands-on experience in our laboratories.

I will continue to use these discretionary authorities to respond to unexpected and pressing public health problems, such as the current epidemic of drug-resistant tuberculosis.

BUILDINGS AND FACILITIES

As you will note from our budget document, the total fiscal year 1993 request for the Office of the Director is $203,430,000. In addition, we have requested $72,518,000 for our Buildings and Facilities appropriation.

The modernization of the Clinical Center began in 1979 as a multi-year program to address the issues of safety, hospital accreditation, and other concerns necessary to assure the delivery of quality of patient care and supporting research. A subsequent study has revealed considerable infrastructure deficiencies with the potential to seriously affect Clinical Center research programs. Therefore, the direction of the existing Clinical Center Modernization Program has been altered to focus on immediate safety issues, to maintain the hospital's accreditation and to correct the most critical infrastructure deficiencies.

Mr. Chairman, I have attempted to give you a picture of the diverse issues and concerns that have engaged the time and energies of me and my staff during my first year as Director of the National Institutes of Health.

In my description of our accomplishments, I hope that I have also been able to convey some of the spirit of striving and animation that has characterized both the Office of the Director and the Institutes this past year. Striving and animation are essential to the health of this powerful enterprise, the NIH. I think that this spirit is very American and has always characterized our national life and our best public institutions.

In 1835, Alex de Tocqueville noted this American spirit. Comparing the life and political institutions of his homeland with the life and institutions he found in the United States, he said, "I will not deny that in the United States one often regrets the absence of those uniform rules which constantly regulate our lives in France. It is no good looking in the United States for uniformity and permanence of outlook. What one does find is a picture of power, somewhat wild perhaps, but robust, and a life liable to mishaps but full of striving and animation."

This concludes my statement, Mr. Chairman. I would be pleased to respond to the Committee's questions.

[The statement of Dr. Healy follows:]

National Institutes of Health
Office of the Director

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[1] Juan Ramon Jimenez, "Heroic Reason," in Selected Writings, trans. by H. R. Hays (New York: Paragon House, 1981).

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This concludes my statement, Mr. Chairman. I would be pleased to respond to your questions.

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[2] Alexis de Tocqueville, Democracy in America, trans. by George Lawrence (Garden City, N.Y.: Doubleday & Co., 1969), pp. 92-93.

BERNADINE HEALY, M.D.

BIOGRAPHY

Dr. Bernadine Healy was appointed by President Bush to be Director of the National Institutes of Health (NIH) in April 1991. As Director of the NIH, she leads a Federal agency that has more than 16,000 employees and an annual budget of approximately $9 billion. In addition to supporting the work of 4,000 scientists located on the NIH campus in Bethesda, Maryland, the agency is the major supporter of biomedical research at universities and hospitals nationwide.

Shortly after her appointment, Dr. Healy launched the NIH Women's Health Initiative, a $619 million effort to study the causes, prevention, and cures of diseases that affect women. She also established the Shannon Award, grants designed to foster creative, innovative approaches in biomedical research and keep talented scientists in a competitive system. Under Dr. Healy's leadership, the NIH is formulating its first Strategic Plan to guide its research efforts into the 21st century.

Prior to her appointment at NIH, Dr. Healy was Chairman of the Research Institute of The Cleveland Clinic Foundation, where she directed the research programs of nine departments, including efforts in cardiovascular disease, neurobiology, immunology, cancer, artificial organs, and molecular biology. From the time of her appointment in November 1985, she also served as a staff member of the clinic's department of cardiology.

In February 1984, Dr. Healy became Deputy Director of the Office of Science and Technology Policy at the White House. Her appointment, made by President Reagan and confirmed by the Senate in June 1984, involved her in life science and regulatory issues at the Federal level. She served as Chairman of the White House Cabinet Working Group on Biotechnology, was Executive Secretary of the White House Science Council's Panel on the Health of Universities, and served as a member of several advisory groups, including the Councils of the National Heart, Lung and Blood Institute, as well as the White House Working Group on Health Policy and Economics.

From June 1976 until February 1984, Dr. Healy was Professor of Medicine at The Johns Hopkins University School of Medicine and Hospital, where she also had clinical responsibilities, directed a program in cardiovascular research, and was Director of the Coronary Care Unit. In addition to serving on the medical school faculty, Dr. Healy assumed the role of Assistant Dean for Post Doctoral Programs and Faculty Development.

Among her other professional affiliations, Dr. Healy has served on the Board of Governors of the American College of Cardiology, served as President of the American Federation of Clinical Research in 1983-84, and was Chairman of the federation's Public Policy Committee for several years. She was President of the American

Heart Association in 1988-89, and has served as a member of its Board of Directors since 1983. As President of the Heart Association, she initiated a Women's Minority Leadership Task Force and a Women and Heart Disease Program that took hold in affiliates nationwide. She is also a member of the Institute of Medicine of the National Academy of Sciences. In 1989, she was elected to a six-year term as a member of the Board of Overseers of Harvard College and has served on the Board of Trustees of Vassar College. She has also been Chairman of the Ohio Council on Research and Economic Development and has served on several other advisory boards, including the Ohio Board of Regents.

Dr. Healy has been active in several Federal advisory groups. Until her NIH appointment, she was a member of the Advisory Committee to the Director of the National Institutes of Health. She has been a member of the White House Science Council and Chairman of the Advisory Panel for New Developments in Biotechnology of the Office of Technology Assessment of the U.S. Congress, as well as a member of the NASA Life Sciences Strategic Planning Study Committee. In 1990, she was appointed to the President's Council of Advisors on Science and Technology (PCAST) and also served as its Vice Chairman. She also chaired the Advisory Panel for Basic Research for the 1990s of the Office of Technology Assessment, and served on the Special Medical Advisory Committee of the Department of Veteran Affairs.

A native of New York City, Bernadine Healy graduated from The Hunter College High School. She received her bachelors degree, summa cum laude, from Vassar College in 1965 and her M.D., cum laude, from Harvard Medical School in 1970. She completed postgraduate training in internal medicine and cardiology at The Johns Hopkins School of Medicine. Dr. Healy has written extensively in the areas of cardiovascular research and medicine, and has served on the editorial boards of numerous scientific journals.

NIH CLINICAL CENTER FACILITIES

Mr. NATCHER. Thank you, Doctor.

Dr. Healy, we discussed with you last week the facilities' problems at the Clinical Center. Are we correct that the funds in the 1993 request for the Center are restricted to emergency repair only?

Dr. HEALY. That is correct, Mr. Chairman.

Mr. NATCHER. As you know, this subcommittee last year turned down the request to begin major renovations in 1992 pending a review by the Corps of Engineers. Briefly now, Dr. Healy, tell us about the review by the Corps of Engineers. What were the findings and how do they address the problems that we have here?

CLINICAL CENTER BACKGROUND

Dr. HEALY. I will start by presenting some background, because I recognize we are talking about an extraordinary amount of money at a time of limited resources. What we do at the Clinical Center must be deliberate and must be careful because it is a lot of money over a long period of time. Also, once we embark upon it, we cannot turn back.

The Clinical Center complex represents one of the most unique facilities for state-of-the-art clinical research. It is the keystone of our intramural program. I believe it is one of the jewels in the entire NIH portfolio. Its design places lab research side by side with patient care activities. It facilitates the rapid transfer of knowledge to the treatment and care of patients. The mixture of science creates an intellectual milieu which stimulates progress in basic and clinical research and creates an environment that I think is unrivaled anywhere.

It is significant that the world's first gene therapy was performed here and the mobilization of Clinical Center resources led to breakthroughs in treatment of AIDS and cancer therapy. The building, which was dedicated in 1952, was a little over 1,000,000 gross square feet. Over the years, there has been addition after addition. The Clinical Center has grown to about 3,000,000 square feet.

Over the years, problems have developed with this kind of approach, mainly in the utility systems, which are of varying ages and conditions and which were not built to meet some of the modem needs of science. The Clinical Center renovation was initiated after our Maintenance Section told us that several of the mechanical systems were no longer able to be maintained. An independent A&E firm indicated that the major utility systems, primarily within the original 1,000,000 square feet of space that provided critical air conditioning, plumbing and ventilation, are outmoded and do not have the capacity to meet the current research and patient care demands.

The electrical systems have exceeded their useful life, significantly increasing the probability of failure. Heating and ventilation capacities are grossly undersized for the size of the building now and fall critically short of providing exhaust for the Center. The air conditioning systems provide only half of the space cooling capacity now required, and asbestos is present.

The independent assessment by the Army Corps of Engineers, which the Committee requested, completely concurred with the NIH findings that there are significant, critical, and, indeed, dangerous deficiencies. It is my impression that the U.S. Army Corps of Engineers concurred in even stronger and more certain terms.

CLINICAL CENTER REPLACEMENT VS. RENOVATION

Over the past two years NIH evaluated a number of concepts. I personally considered four or five possibilities and looked at every possible way to best enhance the modernization and improvement of this complex.

It was finally concluded with unanimity that basic changes are required to cure these deficiencies. There is no question that a major investment needs to be made. What is the alternative? Do we renovate or replace?

Consideration was given to renovating the existing Center. The option was estimated to cost $1,200,000,000. Inherent in this option is the risk to ongoing research programs. It also commits us to a building which evolved from less than a 1,000,000 square foot core with 2,000,000 square feet of space grafted onto it.

The considerable length of time to renovate, 17 years, would be detrimental to the facilities and the research programs. It is not clear that—after 17 years and the enormous investment—we would have a modern facility.

A total replacement facility could be constructed on the NIH campus now. We all agree that best meets our needs. It would cost $1,600,000,000 and take 12 years, not 17 years, to complete. The U.S. Army Corps of Engineers decided that the new facility was the best option.

My original preference was renovation because 1,500,000 square feet of space was built since 1980. That is why it looks so beautiful.

But what I subsequently learned, upon further study and hearing directly about the Corps of Engineers study, was that the facility has a core that is not able to sustain that facility either for research or patient care and renovating indeed might be putting extraordinarily large amounts of good money after bad.

At this point we are also looking at a cost of between $200,000,000 and $400,000,000 over a period of 10 to 15 years in order to go the route of replacement rather than renovation.

I will say one thing that has sobered us all in looking at this. It is that, indeed, this new Clinical Center facility will constitute roughly one-half of all the square footage on the entire NIH campus.

On the campus we have about 7,000,000 square feet of space and 77 buildings. The Clinical Center is 3,000,000 to 3,500,000 square feet of space. This new facility represents preparing the entire NIH campus for the next century. The replacement will be a shorter term project, so it will be more costly on the shorter basis. I think it is difficult not to elect replacement.

CLINICAL CENTER COST ESTIMATES

Mr. NATCHER. Now, Doctor, these cost estimates seem high. How do they compare with similar projects in the private sector? Can you give me some idea?

Dr. HEALY. I come from the private sector. In my previous life, I was involved in the building of two research facilities. I saw, during the period of my involvement, the cost of construction of a research facility go from about $180 to well over $200 per square foot.

We have done a cost analysis and have determined that the cost for this new Clinical Center facility is at $233 per square foot in FY 1992 dollars. This includes discreet activities such as design, design inspection costs, site preparation and relocation costs and the demolition of the existing Clinical Center. To my mind this is certainly within the realm of what the private sector is facing and, if anything, is on the lower side for this kind of very expensive space.

The most expensive space you can build is research laboratory space. It is twice the cost of office space and very close to that of hospital space.

There is another dimension here of which my colleagues remind me. We also have slightly more expensive space because we have greater density in the way we utilize our space. In the private sector it is estimated that there is about 250 square feet per investigator. At NIH we have roughly 177 square feet per investigator. We have the increased programmatic activity. That will entail an increased cost.

I think the $233 cost per square foot that has been estimated is within the bounds of reasonableness.

Mr. NATCHER. What was the basis of the Corps' estimate of the number of patient beds and square footage?

Dr. HEALY. We had to give them guidance on the size of a research hospital. As you know, the NIH Clinical Center is probably the largest research hospital in the world and certainly in this country. We have approximately 50 percent of all dedicated research beds in the entire country in our Clinical Center. The estimates were based on our own anticipated projections in clinical research as we look to the future.

CORPS OF ENGINEER'S RECOMMENDATIONS

Mr. NATCHER. Dr. Healy, what are the main reasons why the Corps recommended replacement rather than renovation as the first choice? Tell us a little now about the issue of ceiling intervals—that is, the difference between 18 and 12 feet ceilings. What do we have here?

Dr. HEALY. I will turn that technical issue over to Mr. Mahoney.

Mr. MAHONEY. Mr. Natcher, that issue relates to the term "interstitial spacing," which is the space necessary to run utilities in a horizontal pattern. The engineers feel that this pattern is a more efficient way to run utilities. The existing Clinical Center does not allow interstitial spacing.

Mr. NATCHER. The Corps of Engineers report says and I quote, "Positive action must be taken at once to avert major system failures at the Center." Do you agree with this statement, Doctor, regarding how soon we should proceed with the work?

Dr. HEALY. I was personally comforted by the Army Corps of Engineers' report because, when I first came to NIH a year ago, I was told we were at risk of some imminent systems' failures, particularly with regard to things you don't see like air conditioning, heating, electricity. I was initially skeptical. What I saw of the Clinical Center, at least on the surface, was a building that looked pretty good.

Unfortunately, my colleagues, who had the benefit of an outside consulting firm and had made a study themselves, told me that the core of the Clinical Center was not constructed to meet the capacity of a modern research facility.

I remained skeptical over several months and kept studying the issue. I kept hearing about chillers and boilers that were in trouble, but, it was not until the Corps of Engineers predicted the conditions of imminent danger that I was persuaded.

So the long answer to your short question Mr. Natcher is, yes, I am now persuaded that this is a pressing need for the NIH campus. I am comforted, considering the magnitude of the investment, that the selected alternative, whether renovation or replacement, will be based on advice from multiple sections and also from people who are independent of any specific NIH institute.

ALTERNATE SOURCES OF FUNDS

Mr. NATCHER. Dr. Healy, do you consider the situation sufficiently serious that the Committee should divert funds from other NIH activities to begin the project in 1993?

Dr. HEALY. As you know, in 1993, we have some money, $7,400,000, which will be used to address some of the immediate needs of the Clinical Center, for example, the sprinkler system, which needs to be upgraded. I think it is unimaginable to ever delay something like that. We have a very dense population in there, some of which are ill patients.

There is no question that imminent danger can be dealt with in 1993. I think it would be helpful, if the Congress, OMB, the Secretary and we agree that we should embark on this replacement sooner rather than later.

Mr. NATCHER. Your budget contains, as you know, about $1 billion for intramural research. What would be your reaction to a temporary reduction in this area in order to free up money for the new building?

Dr. HEALY. I think it would be a very difficult thing to achieve. Most of our intramural budget supports scientists, technicians, and physicians. Probably two-thirds of our budget involves the people doing the business of NIH. I think the only way to get money, even a few hundred million dollars, would be to collapse or contract major programs within NIH, and that would mean, of course, RIFs. You cannot accomplish the downsizing of personnel in time to free up money for such an immediate need.

My additional concern is that downsizing is never temporary. I think that kind of step would be a drastic, if not a draconian, step that would be damaging to the enterprise and very difficult to accomplish, particularly in a year's time.

If you look at our FTEs, you will see that the growth of FTEs in the intramural program has not increased if you exclude the AIDS program. Downsizing would affect that area as well as AIDS research. I do not see either one as a good alternative as it would have a profound effect on our enterprise.

CONSTRUCTION CLAIMS AGAINST NIEHS

Mr. NATCHER. The budget documents indicate that NIH has just been found liable for a $25,000,000 judgment related to the original environmental health facility construction in North Carolina. How will this be paid, and where will the money come from? This money has been paid, as I understand, out of the Treasury. Now it has to come back from NIH. How are you going to do it, Dr. Healy?

Dr. HEALY. We have agreed to pay back the amount at the rate of $4,500,000 a year over five years. We will propose taking the money from our Buildings and Facilities account and we expect to make the first payment this year.

Mr. NATCHER. Mr. Pursell, I yield.

CLINICAL CENTER REPLACEMENT

Mr. PURSELL. I have done a cursory review of the Corps report. I agree that replacement is the answer for the clinical complex.

Mr. Chairman, if you look at the report, the numbers are staggering—$1,600,000,000 for total replacement of the Clinical Center.

I don't know how we are going to resolve this. Is it possible to have the Corps come out during the outside witnesses? Are they scheduled to testify?

Mr. NATCHER. It is possible. We can bring them in.

Mr. PURSELL. I would like to ask more questions on this.

I think you are getting to the heart of the future of the NIH.

The NIH is the jewel of this Committee, and there is not a Member of this Committee who would not sacrifice something else to help in replacing this building.

NIH MASTER PLAN

Mr. PURSELL. The Corp's report said that if there is one single factor that the review committee found to be deficient with regard to the NIH facilities revitalization program, it is the lack of a current master plan. The current use of the master plan is approximately 19 years old, and it is inconsistent with the dynamic nature of the NIH campus.

The absence of a quality, up-to-date plan from which to make future decisions hampers the ability of NIH engineering staff to develop sound and reasonable strategies for future facility use. It is strongly recommended that the master plan process be accelerated to the maximum extent possible to coincide with the planning and design of a facility. Special reports must be exercised to insure that a new master plan is properly maintained and updated on a regular basis. Since you have become the new Director, I am sure you focused on that to some extent.

It would seem to me that the master plan is putting the cart before the horse.

Dr. HEALY. I could not agree more with the Corps. We are talking about a campus with 7,000,000 square feet of space, 77 buildings, 300 acres and lots of ongoing construction.

A master plan is part of strategic planning. It is especially important if we are considering investments of $1,600,000,000 or $1,200,000,000 into redeveloping roughly half the square footage of our entire campus.

Mr. PURSELL. How fast would it be to update the master plan?

Dr. HEALY. We are on a fast track and are in the process of procuring. The final NIH approval will be December 1993.

Mr. PURSELL. So, realistically, we will update the master plan and move along trying to upgrade our facilities without losing some time?

Dr. HEALY. That is correct. Indeed, if we decide to go this route with the Clinical Center, that becomes the cornerstone of the master plan for the entire campus.

OPTIONS FOR THE CLINCIAL CENTER

Mr. PURSELL. I think the Committee owes it to NIH to focus on this as the major agenda before our markup.

I am very hopeful that our influential Chairman will maximize Mr. Early's voice and Carl Pursell's voice and Lou Stokes' and the others to see if there is a way that we can help. That complex is the core of the whole NIH. Those clinical labs are just vital. I don't know if we can afford to delay any longer waiting for a master plan or looking at offsets within the Committee. I don't think that is a good option.

Dr. HEALY. Mr. Pursell, we do not mind looking at any of the hypotheses, including whether we should have a Clinical Center or a research hospital at all. They should all be considered. I think that is a very good exercise because it causes us to consider how important it is for NIH and the community to have a research hospital and an outpatient research facility where people can see that basic research discoveries move to treatment.

Mr. PURSELL. You don't get a good quality program if you try to do everything for everybody. Our priorities and your strategic plan are really on target. I think we have a lot of committee work to do on this to see if we can find our way through this.

Thank you, Mr. Chairman.

Mr. NATCHER. Mr. Early.

WOMEN'S HEALTH INITIATIVE

Mr. EARLY. Dr. Healy, what is the status of the trans-NIH research agenda on women's health which the Office of Women's Health Research is preparing?

Dr. HEALY. That has moved at a fast pace. Dr. William Harlan heads that activity, and it is co-chaired by Dr. Vivian Pinn. The overall design of that study and its three parts has been developed, and it has gone through concept clearance. The community study will be phased-in later.

There have been two public hearings already on the trial. We expect that the RFP will be on the street very shortly, and that, by September, we will be able to award approximately 16 contracts.

OFFICE OF RESEARCH ON WOMEN'S HEALTH

Mr. EARLY. The Committee, for FY 1992, provided a significant increase in funds for the Office of Women's Health and indicated that priority should be given to certain areas such as uterine fibroids, endometriosis and pelvic inflammatory diseases. How much has been allocated for these areas?

Dr. HEALY. Roughly $2,000,000 in co-funded awards, some of which will be in uterine fibroids, endometriosis and other disease areas.

ADDITIONAL FUNDING

Mr. EARLY. Madam Director, this is a general question that is asked all the time. I want you to give serious consideration to it. I agree with Chairman Natcher who always says the NIH budget is the people's budget. He has said that, if he had the money available, he would double it.

My good friend, Mr. Pursell, said the other day in announcing his retirement, which is a loss for all of us, that he would increase the NIH budget to $20,000,000,000.

I know that you are defending the President's budget request. However, if you had a 10 percent increase over the budget request before us now, $1,000,000,000, I would like to know what you would do with that $1,000,000,000.

Dr. HEALY. I am obviously very committed to NIH, and my belief is that NIH represents this country's domestic national security. There are probably three things people want: to be free from foreign invaders; to have some economic security so they can care for their families; and they want their health. I believe NIH plays a vital role in terms of health and in an indirect way in terms of contributing to this nation's economy.

I share your sentiments. I am here to support the President's budget, but if one were to dream or imagine an additional billion dollars——

Mr. EARLY. You say, if one were to dream. I would substitute one that would use common sense.

Dr. HEALY. We would do three or four things.

The top priority would have to be, as I said last year, investing $400,000,000 or $500,000,000 in research project grants. But the way we would do it, if this dream came true, would be to look at some of the areas we and the community views as having strategic importance, like molecular biology, gene therapy, and neurobiology, and we would distribute that grant portfolio in accordance with scientific priorities.

Secondly, I think we have to address the intellectual brain trust at NIH. We have been forced to not increase our stipends. I think a stipend increase between $80,000,000 and $100,000,000 would be important.

I think if we had the resources it would be important to address the problem affecting individuals who have finished their research training and are not yet adequately developed as scientists to be competitive for an RO–1 grant with a 25 percent success rate. This is critical for three or four years for scientists who have nowhere to go to get seed money to start their laboratory.

We could look at a new program such as a junior RO–1 program involving a small grant with institutional co-funding that would help that young scientist get started on an independent scientific career. It is very hard for someone, even if they have been a very successful research fellow, to start out in those first few years.

I also think we are all very committed to the notion of developing programs that would encourage high risk research.

I think if there were additional resources there would be two other considerations we would try to develop. One is attention to the work of the Fogarty Center. We are at a critical time in terms of the changes in the world. We are shifting our national security to what is a peacetime national security. Here, again, the health and stability of the world is very much linked to the economic and physical health of the world's population. There are unique ways that NIH research can help and contribute to that.

Finally, an area that needs some attention is the area of critical technology and instrumentation.

Future advances in understanding the molecular basis of disease is heavily dependent now on very sophisticated and rapidly-developing and changing instrumentation.

In an endeavor like gene sequencing, we need supercomputers and sophisticated robotics. NIH has not had a robust program in bioinstrumentation. It has not invested heavily in bioengineering. NIH has invested on the pharmaceutical side to foster and evaluate drugs in clinical trials, but it has not invested in the evaluation of diseases.

Granted, in development, industry plays a role, investing about another $9,000,000 in research, both in devices and pharmaceuticals. But there is an interface where industry is not going to do the kind of pre-competitive or post-competitive evaluation once an implant or engineering device is in use. We would look to whether or not we would develop and support technology, bioengineering and instrumentation as part of the strategic thinking for the future.

So I think we would have a number of areas where we would co-invest; and we certainly can dream.

USING FOREIGN AID FUNDS

Mr. Early. I am having a hard time extracting an answer to what I asked you. I asked how you would use an additional $1,000,000,000. You did speak of that. I don't want to be facetious, but you said if you had additional money, you would have some interest in increasing funds for the Fogarty Center.

This problem of addressing the clinical center building, and the $1,000,000,000, whether you should go for new construction or not, is a legitimate question.

Couldn't this be viewed as a foreign-aid type of project? Wouldn't it be in the best interest of the whole world to take $1,000,000,000 from the foreign aid budget to build the facility we are talking about to house the programs of the Fogarty Center and all the other institutes?

What about taking $1,000,000,000 from foreign aid, and it is an easy place to take from politically, or even $1,000,000,000 from the defense budget.

The Chairman always talks about the health of the people; $1,000,000,000 from foreign aid for a new clinical center and the Fogarty Center?

Dr. **Healy**. With regard to the Fogarty Center, I think we have to be careful about the figure of $20,000,000, although that is their budget. The vast majority of NIH research contributes to the well-being of the world.

It is in the public domain, and it certainly helps people all over the world, not just people in our own country. The $20,000,000 understates our contributions to the world of science.

In addition to the $20,000,000, there are also grants that go from each of the Institutes to countries outside of the United States. That budget is between $25,000,000 and $30,000,000.

But I do think that at this particular time we might look at, as I said, a high-impact program that would augment the existing programs at the Fogarty International Center.

DESIGN OF CLINICAL CENTER REPLACEMENT

Dr. **Healy**. When you asked me to think about what NIH would do if it had an extra $1,000,000,000, of course, if we came to closure and agreement on the Clinical Center replacement, then there is no doubt in 1993 we would want to put some money into moving ahead with the design. That will be a major project. Design engineers alone will be very expensive.

Mr. **Early**. How much will it be?

Dr. **Healy**. Mr. Mahoney, will you respond?

Mr. **Mahoney**. The range in what would be feasible in 1993, would be between $4,000,000 and $20,000,000.

Mr. **Early**. Thank you, Mr. Chairman.

GAO REPORT ON COMPUTER PURCHASING

Mr. **Natcher**. Dr. Healy, GAO issued a report last fall that was critical of NIH's handling of its computer system contracts. What about this?

Dr. **Healy**. I will ask my colleague, Mr. Mahoney, to answer that question since he is familiar with it.

Mr. **Mahoney**. You are correct, Mr. Chairman, that the GAO was critical regarding the purchase of computers. Their criticism centered on a couple of aspects.

One was that they concluded, and we agree with the conclusion, that we had computer capacity beyond what was needed. There has been an industry-wide reduction in the growth of main-frame computing capacity.

They also suggested that NIH should have a better oversight system with regard to all computers within NIH, and we agree with that.

Finally, they concluded that we should implement a "capacity management program" to better analyze computer capacity.

Just to outline a couple of steps we have taken in response to that report: we have transferred one of the computers. They said we had two beyond our needs. In August, we transferred one of those computers to the National Library of Medicine. They were in the process of purchasing a new computer, so we offset the need for that purchase.

We are in the process of analyzing the necessity for the second computer. We contracted with a company called BGS, Inc., which is a nationally-known corporation skilled in analyzing computer capacity.

They advised against disposing of that second computer at this time until further analysis and tests could be undertaken.

With regard to the oversight criticism, Dr. Healy has requested the establishment of a new position, Director for Information Resources Management, which would oversee a staff dedicated to this area of information resource management.

Mr. NATCHER. Mr. Mahoney, the cover sheet, as you know, on this report, reads "Poor management resulted in unmet scientist's needs and wasted millions." Something that we don't need.

Are you satisfied now, Mr. Mahoney, that this problem has been corrected?

Mr. MAHONEY. Mr. Chairman, I am satisfied that we have taken the corrective steps that will ultimately solve the problem. The establishment of a capacity management program is something that will take some time to develop. In the interim, the Division of Computer Research and Technology that houses the computer center has a new director who has demonstrated very active leadership in correcting this problem.

NIH STAFFING LEVELS

Mr. NATCHER. Dr. Healy, if you would now just briefly, review for the Committee the change in staffing levels at NIH over the last few years.

Dr. HEALY. We have had an amazingly stable work force. We now have 15,000 total FTEs and 15,139 in our 1993 request.

But if you take out the number of FTEs that represent the AIDS FTEs, 1,234, the result is a work force of 13,905, our 1993 request.

Mr. Chairman, in 1981, our work force was 12,637. In 1984, it was 13,661. That suggests that over the decade we have had very little growth in the core of NIH's work force.

Most of the growth has been in response to the terrible AIDS crisis. Even so, I think the growth to 15,000 could be justified, for the most part, by the growth in the NIH budget.

Mr. NATCHER. Your table shows that NIH has added about 2,300 staff over the last five years at an annual cost of $112,000,000. The 1993 budget proposes another 232 positions.

How much control does your office exercise over the Institutes, as far as staffing is concerned, Dr. Healy?

Dr. HEALY. Mr. Mahoney's office tracks the FTEs and has some controls over them. I think in all fairness, there could be a more aggressive monitoring of the FTEs. That is something Mr. Mahoney and I have talked about on several occasions. I think it is something we expect to be looking at over this next year.

Mr. NATCHER. Does NIH have a manpower utilization system in place to determine appropriate staffing levels for various offices and activities, generally speaking?

Dr. HEALY. We have FTE ceilings allocated to the Institutes and then the Institutes decide how to internally allocate their FTEs. I think that there is room for improvement in the way we allocate both space and FTEs. One of the things that is especially difficult to do is to look at a historical base and think about reallocating space or people.

At the present time, we have diagnosed some of the potential soft spots. I have asked Mr. Mahoney and his management staff to proceed with an analysis of it and also some positive ways of controlling growth.

WOMEN'S HEALTH INITIATIVE

Mr. NATCHER. How did you determine the amount of money necessary for the Women's Health Initiative in 1993?

Dr. HEALY. This was based on an analysis of the real cost of the scientific project as it was developed by the planning group. The original estimate, from the concept development stage, was approximately $500,000,000 over 10 years. What we have found is that it will require 14 years and, if you project the costs to 14 years, the total becomes $619,000,000.

So, our original estimates came in amazingly close to the figure from the final budgetary analysis based on the actual scientific design of this large and, indeed, complex study.

Mr. NATCHER. Is there any flexibility in terms of the 1993 amount, if this large an increase is not possible next year?

Dr. HEALY. Once we embark on the clinical trial and the awarding of the 16 centers in this fiscal year, we are obligated to that component of the study. The only flexibility might be to delay further the community study for a few years.

Mr. NATCHER. Has the design and scope of the trial been reviewed by any outside group, such as the National Academy of Science?

Dr. HEALY. It has not been reviewed by the National Academy of Science, but it has had a national concept review and public comment. The concept review is the typical format used by NIH when it is developing a clinical trial or major study of this type.

Dr. Pinn, did you want to elaborate on that?

Dr. PINN. Yes, we have had two concept review meetings, one to review the clinical trial and a second, consisting of a team of people from across the country, representing different institutions and backgrounds, as well as experiences in these types of trials, to review the community trial.

We have received criticism and have responded to it. I feel very comfortable that we are on target with the design of the study and are ready to go forward with the implementation.

Dr. HEALY. Often, as clinical trials of this magnitude develop, the involved scientists, skilled in clinical trials and epidemiology, will take a look at the scientific design and modify it. I have had personal experience in several large muti-center clinical trials and this occurs as part of the review and modification, so it will be a doable trial by the time it enrolls the first patient.

OFFICE OF RESEARCH ON WOMEN'S HEALTH

Mr. **Natcher**. How will you use the $10,000,000 appropriation in 1993, requested for other work at the Office of Women's Health Research?

Dr. **Healy**. That supports the office itself and the variety of programs within the office which includes providing such supplemental and co-funding support to the Institutes and Centers, as discussed with Mr. Early, and also for conducting meetings which are directed at things such as the development and advancement of women in biomedical careers.

The supplemental funding and co-funding on women's issues will be almost $5,000,000. Program support will be $1,000,000. There is also money for workshops such as the one this summer on recruitment, retention, re-entry and advancement of women in biomedical careers.

We are going to have a workshop this fall. There are some initiatives that were mandated by the Congress that will account for another $2,000,000.

SUPPLEMENTAL AWARDS

Mr. **Natcher**. Will this office and the Minority Health Office make their own grants, or will they allocate money entirely through the various institutes?

Dr. **Healy**. If it involves science, the grants are made through the individual Institutes. Often these grants are in the form of a supplemental award. There are some grants to support a particular conference, but that tends to be a small amount of money.

CONSOLIDATED OFFICE BUILDING OCCUPANCY

Mr. **Natcher**. Can you tell us, Dr. Healy, what decisions have been made about which offices and activities will be relocated in the consolidated office building in phases one and two?

Dr. **Healy**. We have developed a plan for which programs will be moving in Phase 1. As you heard yesterday, the National Center for Nursing Research will be moving in its entirety.

What we are trying to do is move in priority order those Institutes where we can consolidate their entire extramural group at one time. That means the smaller Institutes will move in the first phase because we will have only space for 650 FTEs in the first phase of the building.

The larger Institutes, like NINCDS, will not move in until the second phase.

I can submit that for the record. At the present time, there will be probably six Institutes that will be in Phase 1, including the National Center for Nursing Research, NIAMS, NIGMS, and other Institutes.

In the second phase, we are looking at an additional 2,450 people consolidated into the building. That will involve all the Institutes.

[The information follows:]

OCCUPANCY OF THE NATCHER BUILDING

At this preliminary stage of planning, there are six Institutes being considered for Phase I occupancy of the Natcher Building. This includes the entire extramural programs of the National Center for Nursing Research (NCNR), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institute on Deafness and Other Communication Disorders (NIDCD), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Dental Research (NIDR), and National Institute of General Medical Sciences (NIGMS). Since the intention is to move whole Institute programs, it is still possible that one fewer Institute might actually occupy Phase I.

SIZE OF THE CONSOLIDATED OFFICE BUILDING

Mr. NATCHER. What is the square footage of the new building?

Dr. HEALY. Phase 1 and Phase 2 are in the range of 719,000 gross square feet of space. Phase 1 will be 180,000 gross square feet of space.

A substantial part of that will be a lovely conference center. We do not have an auditorium now which is large enough to accommodate the needs of our campus or our extramural community.

We are looking at a conference facility that will have, roughly, a 1,000-person auditorium which can be partitioned into four components, so smaller auditoriums that can be used.

The other aspect of the building is that it will be right across from the Lister Hill Center where we have conferences and auditorium space and the National Library of Medicine.

FUNDS REQUIRED FOR COMPLETION

Mr. NATCHER. How much will be required each year to complete the entire project?

Dr. HEALY. As I mentioned when I appeared before the Committee before, we have money to complete the first phase. That is in total approximately $73,000,000.

In order to complete the entire facility, we need an additional $102,000,000. The $102,000,000 will bring the total cost of the project to approximately $176,000,000.

In 1993, we do not need this money. We could bank it, but we will not need it because we will have the money available to us in the appropriation, that is the $73,000,000.

Mr. NATCHER. What about 1994 and 1995?

Dr. HEALY. That is when we would absolutely need the money to start. Our goal is to start the second phase of this building before the first phase is completed so that we have a continuous project. That will enable us to finish this building by the year 1997. If we can get the money in 1993 or 1994, then we can have the continuity or the timetable that I presented to you.

If we do not get the money until 1995, then we will see a delay in Phase 2 of the project. That could delay it possibly to the end of the decade.

Mr. NATCHER. Dr. Healy, wouldn't it be the best plan to have this money over a period of about three years, the $102,000,000 additional?

Dr. **Healy**. As I understand it, if we extend it to a third year, we get into some procurement problems that would make it necessary to interrupt the project.

What we are trying to strive for is no interruption. Probably the idea would be to have the $102,000,000 distributed over two years or to have it appropriated in 1994, in one lump sum.

Mr. **Natcher**. What I have in mind, would it be better to provide this additional $102,000,000 in equal installments over the period 1993, 1994, and 1995?

Dr. **Healy**. I think I ought to get to you the specific arguments that were presented to me as to why it would have to be by 1994. The technical government rules and regulations I would prefer to present to you and the committee because it involves some technical, legal issues.

Mr. **Natcher**. You do that.

Let us have that information. We will do it right. We don't want a hitch in one year.

You let us know about the others.

[The information follows:]

Funding of the Natcher Building

Funding of the Natcher Building over three years, FY 1993, 1994, and 1995, would require Phase II to be constructed in two stages, extend the currently scheduled completion of the building, and increase the cost of the project by approximately $7.1 million. The first stage of construction would be the underground garage with the second stage being the office buildings. The scheduled completion date on January 1997 would be extended to December 1997 due to awaiting receipt of funding in FY 1995 and the need to have the first stage of construction before beginning the second.

The total estimated project costs would increase from $175.7 million to approximately $182.8 million, an increase of $7.1 million. The increase in cost is due to inflation, separate packages for construction resulting in additional architectural/engineering and construction quality management services, and an increase in construction costs due to phasing.

Specific disadvantages are:

Increased project costs.

Extended completion data.

Two construction procurements with the possiblity of two separate contractors.

Possibility of second contractor voiding warranty work of first contractor.

Potential for cost overruns due to the second contractor not accepting the work of the first contractor and claiming additional costs for repair of construction defects of the first contractor.

Contractor mobilization costs incurred twice.

Dr. **Healy**. We want to have it done by 1997. You and I are going to be there when it is dedicated.

Mr. **Natcher**. You are right.

ESTIMATING REPAIR AND MAINTENANCE COSTS

Mr. **Pursell**. The Corps of Engineers is looking at 3 percent. How do you establish your factor of repair and maintenance cost per facility? Is it based on a replacement cost?

Dr. **Healy**. Yes, it is based upon the replacement cost. The Repair and Improvement request is based upon the National Academy of Sciences recommendations for repair and improvement funding ranging 2 to 4 percent of the facility replacement cost. The NIH funding request uses 4 percent of replacement value for hospital and laboratory facilities, and 3 percent for all other non-research support activities.

Mr. PURSELL. The Corps says our factor is understated.

Dr. HEALY. Yes, the R&I request is somewhat understated. The R&I request only provides for steady-state repairs and improvements and does not include needed funding to address and reduce the backlog of deferred R&I. Likewise the R&I request does not include steady-state funding for non-building facilities outside the five-foot line i.e., underground utilities, roads, etc.

Mr. MAHONEY. Mr. Pursell, the R&I budget is developed primarily on a historical basis. The Corps, as you mentioned, has recommended a percentage of the net replacement value of 2 to 4 percent. As a professional judgment, one would have to concur with that as an approach.

The budget does have a new item in its presentation this year, which is called the Capital Improvement Fund. That is money which is not available until 1994, but it is presented in the 1993 budget and it does provide funds at a level which is consistent with the Corps' recommendations.

Mr. PURSELL. On another page, utilities maintenance and repair, you say the central utilities providing chilled water and steam for comfort and process application, are nearly 40 years old and at the end of their design life.

Dr. HEALY. That is right. The air conditioning serves only half the space it is supposed to serve.

Mr. PURSELL. How big is the backlog? Do we keep a record of backlog?

Mr. MAHONEY. For repairs and improvements that backlog totals about $50,000,000.

Mr. PURSELL. Translate that for me. Is that just for this component?

Mr. MAHONEY. No, that is for the total campus. That will be substantially addressed with the Capital Improvement Fund.

CAPITAL IMPROVEMENT FUND

Mr. PURSELL. Okay.

Is there any way we could move some money over here, Dennis, for a capital outlay?

Are there some options you might present to the Committee outside the NIH budget request?

Mr. WILLIAMS. We have also been concerned over the last number of years about maintaining the capital assets that we have. Because of the budget pressures, we have been very concerned about money going to program first, and secondly, or maybe not at all, to maintaining the capital assets. That is why we did come forward in the 1993 budget with the idea of a Capital Improvement Fund so that we would pay attention to that every year. We want to assure that year in and year out, on a regular systematic basis, we would deal with keeping our assets in an optimum operating level.

Mr. PURSELL. Are there some possible offsets you could review?

Mr. WILLIAMS. The issue of new construction is much more difficult given the numbers we are talking about. We are virtually going to be exploring options just as you will. But there are no obvious sources inside the Department. We are all going to have to decide, I think, on a priority basis what to do, whether we go forward with this and drop other things.

DHHS MASTER PLAN

Mr. Pursell. Do you have a master plan in the Department of Health and Human Services that this fits into?

Mr. Williams. With respect to construction?

Mr. Pursell. Right.

Mr. Williams. We do not have an overall departmental plan. We have encouraged each operating division to develop its own. We do not have a consolidated plan for the Department.

Mr. Pursell. Don't you think you need one?

Mr. Williams. I think it would be a good thing to do.

Mr. Pursell. Maybe you ought to be part of the NIH strategic plan.

Mr. Williams. You make an important point. You cannot make the decisions until you know what the plan ought to be.

In the Social Security Administration, coming before you next week, we have encouraged them to develop a strategic plan. Out of that strategic plan comes some sense of what their capital asset needs are.

We have encouraged the Food and Drug Administration to develop a strategic plan and, hopefully, that will provide an idea of what their needs are as well. NIH is embarked on this, too.

You can not make construction decisions in isolation without knowing where you want to be over a fairly long time.

Mr. Pursell. You leave NIH out there like a lone wolf trying to figure out how to keep up their facilities. The hierarchy of the Department does not have an overall master plan to ensure that we keep the NIH at the state of the art that is necessary for world competition. Maybe that is a policy that you ought to look at down the road.

I would like to ask Dr. Sullivan to go back over the whole budget and see if there are options that we could look at in terms of assisting the NIH in construction. I think it is a high priority.

Mr. Williams. That is a perfectly appropriate thing to ask, not only of Secretary Sullivan, but also of Dr. Mason. It is a question of priorities inside the Federal Government as a whole.

Mr. Pursell. I would rather give up some new personnel and put the money into the construction at NIH.

Mr. Williams. You will find it difficult in the short term to trade off people for construction for the kind of numbers we are looking at. The equation does not balance.

Mr. Pursell. Thank you, Mr. Chairman.

Mr. Natcher. Mr. Early?

WOMEN'S HEALTH RESEARCH

Mr. Early. Dr. Healy, we have talked a lot about women's health. Last year when we talked about women's health, many people on the Floor were talking about earmarking for breast cancer. I see breast cancer as one of the major women's health problems.

This Committee tried to look at the big picture concerning women's health issues. We said we wanted to do more research particularly on uterine fibroids, endometritis and PID.

When I asked you earlier, you said you only spent $2,000,000 for those three areas. Is that adequate?

Dr. HEALY. No. That was only the additional money being placed into those areas within the Office of Research on Women's Health. I can give you the exact figure. It is much more than that.

For breast cancer, the request is $160,000,000, for cervical cancer $24,000,000 and for ovarian cancer $21,500,000. If you add that up, you are looking at over $200,000,000.

EARMARKING FOR BREAST CANCER

Mr. EARLY. Would the Committee, in your professional opinion, be doing the right thing earmarking specifically for breast cancer rather than just women's health overall?

Dr. HEALY. We have seen robust growth by the NCI and NIH over the past few years, in large part because of the focus and concern toward this national epidemic. We have seen a growth that is much faster than in other cancer investments. I think it is appropriate.

I think a $160,000,000 investment in breast cancer is appropriate—that does not include the Women's Health Initiative which has breast cancer as an end point. Probably $10,000,000 of that might be focused on the problems of breast cancer.

In general, I share the view of this Committee that if you earmark with a number like $500 million, it is not driven by a sound analysis of the program need and the portfolio across NIH; is not good management.

You might be force-feeding one area and underfeeding another. If you look at an area like prostate cancer, it is like breast cancer, but it is still behind.

If you look at the area of prostate cancer, it has been woefully neglected. We are increasing our actions in that area.

I think it is dangerous to pull one disease out of the air and say we are going to put this much money into it in one year.

I don't think we can honestly invest $500,000,000 in breast cancer in 1993.

Mr. EARLY. That is my reservation. We sometimes have a lot of demagoguery on the House Floor. It was threatened last year.

When the Chairman brings this bill to the House Floor, if there was an amendment to increase funding for breast from $160,000,000 to $200,000,000, I would want to leave that discretion to the Director.

Right now it is Dr. Healy. In 20 years, it will be someone else. If you don't have a real strong statement, this Committee may get pushed in that direction. I would not vote to earmark $200,000,000 for breast cancer. If you and your directors decided that is where it should be spent, that is fine. If the membership is asked to earmark out of your budget "X" million dollars for breast cancer, they would all put up green lights. I think that would be poor judgment.

Dr. Healy. I agree in the strongest way. That comes from a person committed to seeing we do something about the epidemic of breast cancer. I do not believe that kind of action would strengthen NIH or contribute substantially to the goals we are trying to achieve.

The sentiment we agree with. The earmarking, we do not.

Mr. Early. That was a little easier to extract from you than when I asked you about the additional money. It was very difficult Dr. Healy.

Thank you very much.

Mr. Natcher. Dr. Healy, as you have often heard me say during these hearings, the presentation for NIH have been excellent. We have spent two full weeks now on the hearings and some 25 hours.

All of your directors, the ones who have appeared before our Committee, have given us excellent statements on the budget requests.

The hearings have been excellent. A lot of that is due to you, Dr. Healy, and we appreciate it.

Mr. Pursell?

Mr. Pursell. I fully concur with you, Mr. Chairman.

It has been a great experience and a wonderful opportunity to hear your directors and I welcome your continued leadership, Dr. Healy.

Mr. Early. In my opinion, this to me has been the best presentation by the directors in a long time. They told us what they had.

They told us what the opportunities were in the future. They really did do a good job defending inadequate budgets.

Dr. Healy. Thank you. On behalf of all my colleagues in the NIH leadership, I thank you.

Mr. Natcher. Thank you very much. We appreciate it. We will look forward to marking up this bill. We will mark you up a good bill, Dr. Healy.

The Committee will now recess until 2:00 o'clock this afternoon.

[The following questions were submitted to be answered for the record:]

GRANT APPLICATION HISTORY TABLES

Mr. Natcher. Would you include with the history tables inserted at our overview hearing the Institute specific history table showing numbers of grant applications submitted, approved, and funded as were done last year?

Dr. Healy. The following tables provide numbers of grant applications submitted and funded for fiscal years 1982 to 1993.

Information on approved applications is not included on the table. A Plan for Managing the Costs of Biomedical Research states: "The House and Senate Reports both encouraged NIH 'to modify the peer review system...eliminate the situation where 95% of applications are approved of which only half are really considered as deserving of support.' To remove the semantic confusion, NIH proposed to abolish the practice of 'approving' grant applications. This action would eliminated the category of approved but unfunded applications, i.e., those that contribute to the high 'approval' rate."

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL CANCER INSTITUTE

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1982.........	2,910	748	25.7%
1983.........	3,042	886	29.1%
1984.........	3,029	969	32.0%
1985.........	3,183	1,017	32.0%
1986.........	3,157	953	30.2%
1987.........	3,105	1,061	34.2%
1988.........	2,993	979	32.7%
1989.........	2,913	728	25.0%
1990.........	3,100	728	23.5%
1991.........	3,040	840	27.6%
1992 ESTIMATE	3,184	1,089	34.2%
1993 ESTIMATE	3,137	921	29.4%

NOTE: In the actual years 1982-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL HEART, LUNG AND BLOOD INSTITUTE

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1982.........	2,455	765	31.2%
1983.........	2,519	748	29.7%
1984.........	2,445	852	34.8%
1985.........	2,778	901	32.4%
1986.........	2,822	886	31.4%
1987.........	2,964	966	32.6%
1988.........	2,714	851	31.4%
1989.........	2,716	698	25.7%
1990.........	2,707	675	24.9%
1991.........	2,597	717	27.6%
1992 ESTIMATE	2,639	757	28.7%
1993 ESTIMATE	2,548	777	30.5%

NOTE: In the actual years 1982-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF DENTAL RESEARCH

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1982.........	386	108	28.0%
1983.........	333	133	39.9%
1984.........	372	123	33.1%
1985.........	381	131	34.4%
1986.........	451	151	33.5%
1987.........	456	130	28.5%
1988.........	449	114	25.4%
1989.........	456	109	23.9%
1990.........	499	105	21.0%
1991.........	432	132	30.6%
1992 ESTIMATE	454	103	22.7%
1993 ESTIMATE	450	111	24.7%

NOTE: In the actual years 1982-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1982.........	2,289	645	28.2%
1983.........	2,210	777	35.2%
1984.........	2,247	785	34.9%
1985.........	2,462	786	31.9%
1986.........	1,923	637	33.1%
1987.........	1,803	686	38.0%
1988.........	1,868	594	31.8%
1989.........	1,913	504	26.3%
1990.........	1,844	425	23.0%
1991.........	1,922	518	27.0%
1992 ESTIMATE	2,194	638	29.1%
1993 ESTIMATE	2,098	562	26.8%

NOTE: In the actual years 1982-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover. Data reflects the establishment of NIAMS in 1987 with comparable adjustment for FY 1986.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1982.........	1,717	500	29.1%
1983.........	1,785	539	30.2%
1984.........	1,908	564	29.6%
1985.........	2,127	722	33.9%
1986.........	1,892	643	34.0%
1987.........	1,769	697	39.4%
1988.........	1,504	596	39.6%
1989.........	1,556	493	31.7%
1990.........	1,688	409	24.2%
1991.........	1,582	474	30.0%
1992 ESTIMATE	1,698	442	26.0%
1993 ESTIMATE	1,749	449	25.7%

NOTE: In the actual years 1982-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover. Data reflects the establishment of NIDCD in 1989 with comparable adjustment for FY 1988.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1982.........	1,550	411	26.5%
1983.........	1,519	522	34.4%
1984.........	1,498	507	33.8%
1985.........	1,635	549	33.6%
1986.........	1,713	549	32.0%
1987.........	1,881	641	34.1%
1988.........	2,076	636	30.6%
1989.........	2,165	652	30.1%
1990.........	2,286	627	27.4%
1991.........	2,048	641	31.3%
1992 ESTIMATE	2,367	541	22.9%
1993 ESTIMATE	2,484	627	25.2%

NOTE: In the actual years 1982-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1982.........	2,330	859	36.9%
1983.........	2,188	835	38.2%
1984.........	2,113	702	33.2%
1985.........	2,299	987	42.9%
1986.........	2,446	981	40.1%
1987.........	2,258	857	38.0%
1988.........	2,709	1,044	38.5%
1989.........	2,781	788	28.3%
1990.........	2,826	623	22.0%
1991.........	2,499	874	35.0%
1992 ESTIMATE	2,901	905	31.2%
1993 ESTIMATE	3,067	814	26.5%

NOTE: In the actual years 1982-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1982.........	1,599	439	27.5%
1983.........	1,607	452	28.1%
1984.........	1,661	415	25.0%
1985.........	1,880	469	24.9%
1986.........	2,048	490	23.9%
1987.........	1,642	545	33.2%
1988.........	1,829	450	24.6%
1989.........	1,762	433	24.6%
1990.........	1,610	311	19.3%
1991.........	1,461	370	25.3%
1992 ESTIMATE	1,705	422	24.8%
1993 ESTIMATE	1,772	444	25.1%

NOTE: In the actual years 1982-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL EYE INSTITUTE

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1982.........	643	273	42.5%
1983.........	597	247	41.4%
1984.........	660	309	46.8%
1985.........	788	367	46.6%
1986.........	779	362	46.5%
1987.........	632	313	49.5%
1988.........	645	277	42.9%
1989.........	724	310	42.8%
1990.........	674	254	37.7%
1991.........	752	247	32.8%
1992 ESTIMATE	809	248	30.7%
1993 ESTIMATE	850	231	27.2%

NOTE: In the actual years 1982-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1982.........	411	104	25.3%
1983.........	277	98	35.4%
1984.........	323	138	42.7%
1985.........	389	108	27.8%
1986.........	417	107	25.7%
1987.........	447	129	28.9%
1988.........	400	114	28.5%
1989.........	378	100	26.5%
1990.........	367	104	28.3%
1991.........	374	103	27.5%
1992 ESTIMATE	443	129	29.1%
1993 ESTIMATE	441	125	28.3%

NOTE: In the actual years 1982-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE ON AGING

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1982.........	699	175	25.0%
1983.........	721	152	21.1%
1984.........	645	129	20.0%
1985.........	752	209	27.8%
1986.........	820	205	25.0%
1987.........	726	201	27.7%
1988.........	843	214	25.4%
1989.........	821	194	23.6%
1990.........	882	192	21.8%
1991.........	1,063	329	31.0%
1992 ESTIMATE	1,160	303	26.1%
1993 ESTIMATE	1,257	243	19.3%

NOTE: In the actual years 1982-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1986.........	651	199	30.6%
1987.........	628	179	28.5%
1988.........	720	188	26.1%
1989.........	702	185	26.4%
1990.........	743	149	20.1%
1991.........	719	228	31.7%
1992 ESTIMATE	825	194	23.5%
1993 ESTIMATE	833	184	22.1%

NOTE: In the actual years 1986-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1988.........	262	104	39.7%
1989.........	254	97	38.2%
1990.........	350	130	37.1%
1991.........	436	135	31.0%
1992 ESTIMATE	517	117	22.6%
1993 ESTIMATE	588	141	24.0%

NOTE: In the actual years 1986-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL CENTER FOR RESEARCH RESOURCES

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1990.........	125	27	21.6%
1991.........	126	38	30.2%
1992 ESTIMATE	135	26	19.3%
1993 ESTIMATE	155	27	17.4%

NOTE: The estimates for 1991 and 1992 do not include anticipated carryover.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL CENTER FOR NURSING RESEARCH

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1986.........	217	48	22.1%
1987.........	160	48	30.0%
1988.........	193	52	26.9%
1989.........	264	50	18.9%
1990.........	290	48	16.6%
1991.........	255	50	19.6%
1992 ESTIMATE	319	44	13.8%
1993 ESTIMATE	343	53	15.5%

NOTE: In the actual years 1986-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover.

DHHS-NATIONAL INSTITUTES OF HEALTH

NATIONAL CENTER FOR HUMAN GENOME RESEARCH

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1989.........	129	41	31.8%
1990.........	163	38	23.3%
1991.........	195	75	38.5%
1992 ESTIMATE	231	43	18.6%
1993 ESTIMATE	284	91	32.0%

NOTE: In the actual year 1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover.

DHHS-NATIONAL INSTITUTES OF HEALTH

SUMMARY - NIH

Number of Competing Research Project Grants

YEAR	NUMBER REVIEWED	NUMBER FUNDED	SUCCESS RATE
1982.........	16,989	5,027	29.6%
1983.........	16,798	5,389	32.1%
1984.........	16,901	5,493	32.5%
1985.........	18,674	6,246	33.4%
1986.........	19,336	6,211	32.1%
1987.........	18,471	6,453	34.9%
1988.........	19,205	6,213	32.4%
1989.........	19,534	5,382	27.6%
1990.........	20,154	4,845	24.0%
1991.........	19,501	5,771	29.6%
1992 ESTIMATE	21,581	6,001	27.8%
1993 ESTIMATE	22,056	5,800	26.3%

NOTE: In the actual years 1982-1990, the total eligible for funding includes the council recommended for approval plus unfunded carryover from the prior year. The estimates for FY 1991 and and FY 1992 do not include anticipated carryover.

NORTH CAROLINA ENVIRONMENTAL HEALTH FACILITY

Mr. Natcher. Was NIH found negligent in its handling of this contract?

Dr. Healy. The design of the NIEHS permanent facilities in Research Triangle Park, North Carolina, was administered by representatives of the Facilities Engineering and Construction Agency (FECA), Office of the Secretary, Department of HHS. The FECA has since been disbanded by the Department. The Department's Region IV Engineering Office awarded a construction management contract to Turner Construction with a guaranteed maximum price of $65.4 million established in May 1977. Neither the design nor the construction contract was administered by NIH.

Trouble occurred almost immediately after the start of construction with the greatest problems related to the interstitial spaces (areas set aside to house the building's complex utility systems between laboratory floors). The contractors claimed that they could not fit all the heating, ventilation, air conditioning, and electrical equipment in the interstitial spaces as shown on the design documents. An attempt to do so would result in an unacceptable cramped and crowded utility space. Because of the time delays that resulted from resolving this problem, the project required 66 months, rather than the contracted 33 months, to accomplish and many of the subcontractors as well as Turner filed claims.

After a seven month trial, four and a half year wait, for decision, the Armed Services Board of Contract Appeals (ASBCA) ruled for the contractors. With respect to liability, the ASBCA stated in its published decision of January 10, 1990:

> "The Government's liability arises under its contract with Turner, the terms of which were passed on to subcontractors, either because the contract or specifications were defective or the performance of the subcontractors was affected by actions or inactions by Government agents".

Because of the possibility of lawsuit by the Department against the firm which prepared the specifications and drawings, it would be inappropriate to comment whether the Board's finding places blame upon the Government per se.

DIRECTOR'S 1 PERCENT TRANSFER AUTHORITY AND DISCRETIONARY FUND

Mr. Natcher. Doctor Healy, the Budget requests a modification in the 1 percent transfer authority to allow broader use of these funds. Why is this necessary?

Dr. Healy. A change is requested to provide transfer authority for high priority activities as the Director may so designate, in lieu of the current transfer authority for emergency activities. This change will allow the Director more flexibility to apply funds to meet significant research opportunities and high priority initiatives.

Mr. Natcher. Are there any specific issues in 1992 which you think would justify use of the transfer authority which do not qualify as emergencies?

Dr. Healy. In FY 1991, the James A. Shannon Award program was initiated to provide a discrete limited award to investigators whose priority scores fall just short of the cut-off for funding. The Shannon Awards allow investigators to demonstrate their research capabilities and lend additional weight to meritorious applications. In 1991, NIH funded 310 Shannon Awards, through a combination of funds from the Director's Discretionary Fund ($14.5 million) and the transfer authority ($15.5 million). In 1992, NIH could fund at most only 185 awards, using the total Director's Discretionary Fund. In FY 1992, we will not be able to use the transfer authority as was done in FY 1991, because the Shannon Award initiative does not meet the "Emergency" criteria placed on the FY 1992 transfer fund authority. The average cost for these awards was $100,000 in FY 1991 and will be the same for FY 1992.

This new program has been well received by the research community and has allowed for awards made across the full spectrum of NIH programs, including studies on estrogens in older women, breast cancer receptor patterns, recovery after myocardial infarction, and drug-resistant HIV in children. Use of the one percent transfer authority would have allowed NIH to continue this important new mechanism of research support at the 1991 level.

Mr. Natcher. What can you tell us about your current plans for Shannon awards in 1992 and 1993?

Dr. Healy. We are currently reviewing the success rate for R01 awards as well as ways in which my FY 1992 discretionary funds can best be used. The Shannon Awards are a priority and we plan to fund as many as possible in FY 1992 and FY 1993. In FY 1992, we will not be able to use the $15 million used from my transfer authority as was done in FY 1991, because the Shannon Award initiative does not meet the "Emergency" criteria placed on the FY 1992 transfer fund authority.

Mr. Natcher. How much of your $20 million discretionary fund will be used for Shannon awards in 1993?

Dr. Healy. No final decisions have been made. I am examining all the appropriate needs placed on these funds. However, I consider the Shannon Awards a high priority and plan to fund as many as possible with these funds.

Mr. Natcher. Doctor Healy, why haven't funds been included separately in the regular 1993 budget request for Shannon awards?

Dr. Healy. The Shannon Awards were not included as a regular item in the 1993 budget request because the award was not intended to be a permanent award program. It was a temporary measure resulting from the low success rate of the traditional NIH grant application and the concomitant low morale of scientists. This was a particular problem with young scientists who were frustrated by their inability to begin independent research careers and senior scientists who were frustrated by the difficulty in acquiring funding for their meritorious projects that fell on the "margin of funding." Once the success rate for R01 awards is 35% or better, I do not anticipate a need for continuing the Shannon Awards.

BUDGET REQUEST BY MECHANISM

Mr. Natcher. Doctor Healy, as you know, the Subcommittee has traditionally used this last hearing as an opportunity to review with the Director some of the cross-cutting issues which have been raised with the individual Institutes. As I said to the Secretary, the President's overall request is a good beginning for NIH with an increase of about 5% in very difficult times. Having said that, the Members sitting here can't help but express concern about the lack of balance in the way this budget is distributed among NIH programs. The President's budget provides a decent increase for grants and in-house activities but it freezes funding across the board for every other mechanism. We would both like to add a lot of money to this request. But, if we can't, should the Subcommittee rearrange some of this money to create a better balance?

Dr. Healy. In NIH's FY 1993 President's Budget, 21 percent of the $441 million increase is available for mechanisms other than research project grants. Certain mechanisms, such as research training, R&D contracts, and most centers will be funded at the FY 1992 level.

By funding our highest priorities (research project grants, the Minority Health Initiative and the Women's Health Study) we were unable to provide real growth in almost all of the other non-research project grant mechanisms of support. We believe this balance represents NIH's best judgment as it affects the distribution of funds available in these times of economic constraint.

MINORITY HEALTH EMPHASIS AND REPORTING

Mr. Stokes. Last year, in the report accompanying this bill, the Committee directed the Secretary to require each Institute to report annually to Congress through a consolidated report, approved by the Secretary, on activities in the area of minority health. The Committee also indicated that the report currently produced by the National Institute of Allergy and Infectious Diseases could be a model for such a report. Where is NIH and the Department in terms of preparing this report?

Dr. Healy. The consolidated report on NIH activities in the area of minority health, Strengthening Minority Health Research and Research Training Activities at the National Institutes of Health, was completed in January 1992 and submitted to the Secretary for final approval. The Secretary's office returned the report with comments shortly thereafter. We have not yet submitted a revised report.

Mr. Stokes. When will it be finished and submitted to the Committee?

Dr. Healy. Once we have revised the report and the Secretary's office has cleared it, the report will be submitted to the Committee.

WOMEN AND MINORITIES IN THE EXTRAMURAL GRANT PROCESS

Mr. Stokes. During the NIH overview hearing which was conducted on March 12, I asked you about the amount of competing and noncompeting awards which have gone to women researchers. When I asked you if similar information was available with reference to minorities, you indicated that this information is very difficult to obtain, reading from the transcript, you said: "We have information by race only on a more limited basis. It is easier to identify gender by the name. Identification of race is self-identification. It is voluntary. And we do not compile that data in a total sense, so we cannot give you the same kind of data that you have there on race groups." Do you recall our conversation? In fact, I raised this issue last year, and the response from NIH basically was the same.

Dr. Healy. Yes, I do recall that conversation.

Mr. Stokes. Before moving on, let me ask you this, the NIH's budget for 1993 is about $9.3 billion -- is that correct?

Dr. Healy. Yes, NIH's total FY 1993 Request is $9.376 billion.

Mr. Stokes. Of this amount, how much and what percentage of the budget supports extramural research?

Dr. Healy. Of this amount, $7.513 billion, or 80.1%, supports extramural awards if you include funds associated with the extramural programs of the Cancer Prevention and Control and the National Library of Medicine components of the NIH budget.

Mr. Stokes. I still have some questions regarding this issue. Your office has indicated to me on numerous occasions that race-specific data are very difficult to obtain, making it almost impossible to ascertain the level of participation of minorities in the extramural process. Issues related to discrimination and accuracy have been said to be barriers. Are you familiar with a NIH publication titled: "Women in NIH Extramural Grant Programs?" This publication was put together by the Management Information Services Unit of the Statistics, Analysis, and Evaluation Section. It reviews extramural grants awarded from 1981 to 1990.

Dr. Healy. Yes, I am familiar with the NIH publication titled: "Women in NIH Extramural Grant Programs".

Mr. Stokes. Have you read this publication?

Dr. Healy. Yes, I have read the publication.

Mr. Stokes. On page 7 of the report, it is stated that "A principal investigator submitting an application for an NIH research grant is usually asked to submit information on race, gender, and age as part of his or her application." The report goes on to explain how this information is processed. Responses to this type of question are voluntary, is that correct?

Dr. Healy. Yes, responses are voluntary.

Mr. Stokes. Do you know how many and what percentage of applicants respond to this question as it relates to race?

Dr. Healy. As stated on page 10 of the report, in 1990 71 percent of applicants responded to the race question.

Mr. Stokes. How about to sex? (Page 10 of the report shows a set of graphs which indicate that 71 percent of the applicants identified themselves on a race basis; whereas, 74 percent of the applicants identified themselves on the basis of sex.)

Dr. Healy. As stated on page 10 of the report, in 1990 74 percent of applicants responded to gender.

Mr. Stokes. Based on the information contained on page 10 of this publication, it is clear that responses based on race and gender are about the same. Nonetheless, in one instance (as the data relate to women researchers) you have put together a comprehensive report of this nature; while, in the other (as the data relate to minorities) you have not. Why has NIH not compiled a similar report on extramural grants awarded to minority researchers?

Dr. Healy. This report was started as "Women and Minorities on NIH Extramural Programs". In order to publish in a timely manner, the womens portion was published separately. The minority portion is being designed. DRG published "DRG Peer Review Trends" which includes some minority data at the present time.

Mr. Stokes. My office has spoken with one of the researchers who prepared the women's report. We have been told that a similar report could be compiled with little difficulty. Based on this information, would you support the compilation of a similar report for minorities. (They indicated that they have not yet compiled it because they did know what type of interest there was in this type of information) What level of funding would be required, and how long would it take to prepare a similar document?

Dr. Healy. It is expected that a similar report for minorities will be completed by the end of 1992. Additional funding would not be required in order to prepare the report.

SUPPLEMENTAL AWARDS

Mr. Stokes. I addressed the issue of supplemental awards during the overview hearings also. You indicated that efforts have been taken to advertise the availability of these awards, and that the response has been good. If I recall correctly, you indicated that 659 supplemental grants have been provided -- is that correct?

Dr. Healy. Yes. In FY 1991, the NIH made 398 new minority supplemental awards and 261 continuing awards, for a total of 659.

Mr. Stokes. Recently, my office has learned that some who have applied for these grants, individuals deemed to have meritorious applications, have been denied awards in this area. In one case, I am told, an application was submitted to NIAID, and funding was denied because there was only enough funding to support three applications, and the institute had received 11 requests. What is the general NIH policy regarding allocations for the minority supplement program?

Dr. Healy. The policy of the NIH is to make as many supplemental awards as possible with the available funds, provided that the applications meet the prescribed criteria. These include: eligibility of both the grant to be supplemented and the proposed minority participant; the potential for the supplemental funding to both enhance the research capability of the participant and strengthen the existing research program; and the maintenance of program balance and priorities of the funding component. During the approximately two years that the supplement program has been in effect, each funding component has allocated sufficient funds to award a high percentage of the applications received. In FY 1991, the overall success rate for this program was 76 percent.

Mr. Stokes. Are there funds which are specifically allocated in your budget, or the individual institute budgets for this activity?

Dr. Healy. Neither the Office of the Director nor the funding components of the NIH have made specific budgetary set asides for this program, although the individual budget breakdowns do include funds for noncompetitive supplements, a category that includes the minority supplements. The program has been underway for only a little over two years, and, at the outset, the NIH had no way to determine what the response would be. In addition, the supplement program recruits minority individuals from the high school level through college, pre- and postdoctoral to the investigator level, with the costs differing considerably from level to level. As the program matures, the funding components will be better able to make specific budget estimates for future years.

Mr. Stokes. How much and what percentage of the NIH budget was provided for this activity in FY 1992?

Dr. Healy. As noted above, none of the funding components of the NIH set aside funds in the budget specifically for the minority supplement program. The general category for noncompeting supplements in each budget includes funds available for the program.

Mr. Stokes. What level is proposed for FY 1993?

Dr. Healy. As noted above, it is not separated from the general category for noncompeting supplements in each budget.

Mr. Stokes. Funds awarded for minority supplements represent what percentage of expenditures of eligible research grants? (less than 1 percent)

Dr. Healy. In FY 1991, the NIH awarded a total of 659 minority supplements for a total of $20.6 million dollars. Dollars awarded for the 12 categories of research grants eligible for minority supplements totalled $4.5 billion dollars. Thus the minority supplement program comprised 0.46 percent of the total expenditures for this group of awards.

Mr. Stokes. How many applications were received in the last two most recent years for which you have data?

Dr. Healy. Complete data are only available for FY 1991. In that year, the funding components received 524 applications for minority supplements.

Mr. Stokes. How many were funded?

Dr. Healy. Of the 524 applications that were received, 398 (76 percent) were funded. In FY 1990, the NIH made a total of 376 minority supplement awards (267 new and 109 continuing).

Mr. Stokes. Of the total number received, how many competed successfully, but did not receive funding?

Dr. Healy. A high percentage of the 126 applications which were disapproved were deficient in meeting one or more of the criteria for funding. Only a small number of the applications were not funded solely due to lack of available funds. The exact breakdown is not available at this time.

MINORITY HEALTH INITIATIVE

Mr. Stokes. The budget requests $45 million to establish the Minority Health Initiative in FY 1993. According to the justification, of this amount, $25 million will be used in support of a minority biomedical training program. The justification specifically refers to "Community and Junior Colleges; Minorities in

Majority Schools; the M.S./Ph.D Training Program; and Extramural Associates Graduates Awards." No reference is made to HBCU's, particularly their undergraduate programs. (page 285) Why was reference to HBCU's omitted from the justification?

Dr. Healy. HBCU's are essential participants in all the Minority Health Initiative and Biomedical Training Programs established and implemented by the NIH Office of Minority Programs (OMP). Specific opportunities for HBCU participation include the following OMP minority biomedical training programs:

The M.S./Ph.D. Program that provides opportunities for minority students pursuing a master's degree in a biomedical field at a minority institution, including an HBCU, to continue their training in a Ph.D. program.

The Community and Junior College Program developed as a second "bridge" program that will ease the transition between two-year colleges and four-year colleges for minority students eager to pursue a biomedical sciences career path. This would pave the way for two-year graduates to enroll in an HBCU after obtaining their associate degree.

The Pre-College/Undergraduate Intervention Program that establishes a new academic enrichment intervention program for pre-college and undergraduate students. HBCU's can be significant participants in this program in several ways.

- By serving as host sites for consortia of academic institutions that provide academic enrichment in the biomedical sciences to pre-college students and their teachers;
- By providing laboratory experiences for undergraduate students, particularly freshman and sophomore students who may still be undecided about an academic major;
- By offering hands-on in-service training to middle school and high school science teachers.

Mr. Stokes. To what extent will HBCU's participate in this initiative?

Dr. Healy. HBCU's are full participants in OMPs efforts to strengthen minority biomedical training. HBCU's graduate a substantial share of minority students who pursue careers in the biomedical field, thus it is imperative that programs and funds are targeted at those institutions if NIH is to achieve its goal of producing more minority biomedical scientists. Specifically, HBCU's will participate in the following ways:

1. M.S.-Ph.D. Program. This "bridging" program will provide opportunities for minority students pursuing a master's degree in a biomedical field at a minority institution, including an HBCU, to continue their training in a Ph.D. program. Through this program, formal linkages will be established between HBCU's and Ph.D.-granting institutions that will ease the transition between the

master's and Ph.D. programs. We anticipate that many HBCUs will take the lead role in establishing the partnerships with Ph.D.-granting institutions.

2. Community and Junior College Program. This second "bridge" program will ease the transition between two-year colleges and four-year colleges for minority students eager to pursue a biomedical sciences career path. HBCUs will undoubtedly be key participants in this program, particularly through extensive outreach efforts to the junior and community colleges.

3. Pre-College/Undergraduate Intervention Program. NIH has collaborated with the National Science Foundation to establish a new academic enrichment intervention program for pre-college and undergraduate students. Building on their strong track record in working with elementary and secondary school students and teachers, HBCU's will be full partners in our efforts to attract more young minority students into the biomedical sciences.

Mr. Stokes. What other initiatives will be supported with this increase?

Dr. Healy. The balance of funds will be used in minority lifespan issues that include research on infant mortality, health behaviors of adolescent and young adult minorities, and the health problems of older minorities Americans.

Mr. Stokes. To what extent will these initiatives address the disparate incidence of disease and disability in minority communities? (Particularly, those diseases identified in the 1985 Heckler Report...Diabetes, Heart Disease and Stroke, Infant Mortality, Homicide and Other Injuries, Cancer, and Chemical Dependency)

Dr. Healy. The Minority Health Initiative directly targets those health issues that are of greatest concern to minority Americans. Indeed, the Fact-Finding Team report cited the diseases and disabilities mentioned in the Heckler Report, and called for a reduction in the burden of illness among minority populations to a level equal to that of the general population by the year 2000. The Minority Health Initiative includes the following programs that cover the lifespan and are aimed at preventing chronic diseases and reducing death rates stemming from these conditions:

1. **Cooperative Community-based Perinatal Studies and Interventions in Minority Populations.** The Office of Minority Programs is collaborating with the National Institute of Child Health and Human Development (NICHD) and the National Center for Nursing Research (NCNR) to implement a comprehensive program. The objective of this initiative is to implement comprehensive programs to address the high rate of infant mortality and low birthweight among Blacks in Washington, D.C., using epidemiological, sociological, and clinical approaches. An important component of this program is community-based interventions to test improved methods of outreach to encourage early entry into prenatal care, more acceptable health care delivery, social support and behavioral

interventions to address factors contributing to infant mortality. Our efforts in Washington, D.C. will serve as a model for similar efforts across the U.S.

2. **Minority Youth Health Behavior Research: The Development and Evaluation of Interventions**. The Office of Minority Programs, in collaboration with 10 ICDs, developed and implemented an NIH-wide initiative to address the specific health needs and concerns of minority youth. There is an emphasis on violence and the sequelae of sexual behavior because these account for a great deal of the disparity in minority youth health. The initiative also includes intervention programs for health and disease conditions that affect minority youth ages 10-24. An example of a community- or school-based intervention program may include components of other health behavior, such as nutrition, dental care, asthma control, obesity or diabetes. As a cooperative agreement, grantees will work together to increase comparability across sites. A separate data coordinating center will provide analytical support within sites and facilitate comparative analyses. This initiative will be funded through the OMP.

3. **Health Behaviors of Young Adult Minorities**. The Office of Minority Programs is implementing an NIH-wide initiative to address these health problems of young adult minorities, ages 24-39. The basic approach will be a periodic health screening evaluation, with outreach for minorities in that age group. An integral component of intervention is education to enhance adherence to prescribed treatments or preventive behavioral interventions, as well as follow-up. Initial discussions with ICDs have begun, exploring the possibility of collaboration with asthma centers, diabetes programs, and others in preparation for issuing an RFA.

4. **Problems of Older Minority Americans**. There are statistical gaps regarding the nature and extent of morbidity and disability in older minority individuals. Recognizing the need to address these gaps, the National Institute on Aging issued a RFA on physical frailty in older minority populations in FY 1991. The objectives focus on factors affecting the severity and progression of chronic diseases and conditions in minority populations as well as the relationship of disease severity to specific types of functional impairment. The Office of Minority Programs will collaborate with NIA to fund additional projects to develop and test intervention strategies for dealing with various frailties.

5. **HHS Secretary Sullivan's Minority Male Initiative**. In March 1990, HHS Secretary Louis Sullivan announced an initiative to address the major health problems confronted by minority males. The initiative has four primary objectives:

- To provide a public forum for the problems that minority males face in communities throughout the nation;
- To fund programs in health promotion, violence prevention, criminal justice, drug abuse prevention and treatment, HIV risk reduction and family support;

- To work with agencies at federal, state and local levels to assure that their programs include components designed to meet the needs of minority males;

- To encourage public/private partnerships so that information and resources can be shared and successful minority male programs expanded.

OMP is participating in the continuation and expansion of Secretary Sullivan's Minority Male Initiative. The program is a jointly funded effort of the four HHS operating divisions -- the Public Health Service, Administration on Children and Families, Health Care Financing Administration, and Social Security Administration.

In addition to those specific health initiatives, the minority training initiatives cited above are directly related to addressing the disparate incidence of disease and disability among minorities. NIH believes that the addition of more minority biomedical scientists will have positive effects. The great challenge facing this nation is translating research knowledge into practical application in the minority community. Minority biomedical scientists, health officials and physicians are uniquely positioned to take the science directly to the people.

OFFICE OF RESEARCH ON WOMEN'S HEALTH

Mr. Stokes. I would like to welcome Dr. Vivian Pinn. She has a most distinguished record. Dr. Pinn, what are some of the priority areas which will be supported by your office?

Dr. Pinn. In the first year of operation, the Office of Research on Women's Health (ORWH) established the basis for the research agenda on women's health and in the second year designed and is implementing that agenda: The ORWH Research Agenda on Women's Health.

The ORWH Research Agenda on Women's Health directs research efforts aimed at promoting and enhancing health and preventing and/or controlling disease among women across the life span, from before birth to old age. The agenda will be accomplished through research efforts encompassing biomedical and biobehavioral research spectrum from basic science through clinical trials to community demonstration and education studies. Diseases or conditions that have not had sufficient research attention (for example, coronary heart disease, AIDS, menopause) or diseases or conditions among certain groups of women (such as minority or underserved groups) which have not received sufficient research attention will be addressed. For example, the Office will address diseases that have a greater prevalence or have a particularly devastating effect in minority women, such as systemic lupus erythematosus, diabetes, AIDS, hypertension and stroke, fibroids, pelvic inflammatory disease, and others. In addition, attention to those diseases and conditions identified by the Congress will be addressed; uterine fibroids, endometriosis, pelvic inflammatory disease, relationship between oral contraceptive use and breast cancer, women and AIDS, and the status and ongoing health effects of those exposed to the synthetic estrogen drug DES. As always, the Office will consider the implications of these diseases for both majority and minority women.

During its second year of operation (FY 1992), the ORWH is directing approximately $7 million toward those diseases and conditions specified in The ORWH Research Agenda on Women's Health: $5 million in administrative supplements and co-funding and $2 million for special high priority projects such as an 1992 RFA, co-funded by the ORWH and the National Institute of Child Health and Human Development, addressing state of the art fibroid and endometriosis research of clinical importance, particularly as it relates to minority women where the prevalence of fibroids is higher than among majority women.

Mr. Stokes. To what extent will you be working with the Institutes and the Office of Minority Health?

Dr. Pinn. The Office of Research on Women's Health (ORWH) works closely with the Office of Minority Programs (OMP) on issues relevant to both minorities and women. Both Offices co-chaired the Committee on the Scientific Initiative -- Women, Minorities, and the Underserved -- contained within the NIH Planning Document as well as the Committee on the Inclusions of Women and Minorities in Clinical Research. Preliminary discussions have been held to consider offering joint funding for directed research on minority women to one or more of the NIH Institutes.

Both the ORWH and the OMP work through the Institutes, Centers, and Divisions (ICDs) of the NIH to fund research relevant to women and minorities. As such, it is incumbent upon all these groups to assure that a strong and forceful agenda directed toward women and minorities is implemented in an efficacious and expeditious manner. Thus, the ORWH works with these groups in three major ways. First, the ORWH works individually with the ICDs to implement The ORWH Research Agenda on Women's Health. This is an intensive collaboration to embed this mandated research agenda within the individual ICDs. This also represents an important opportunity to assure that both majority and minority women are appropriately represented. For example, the ORWH is in discussion with the National Institute on Musculoskeletal, Arthritis, and Skin Diseases to consider enhancing their osteoporosis portfolio to include a stronger outreach to minority women who were previously thought not to be affected by this disease. Second, the ORWH works collaboratively with all the ICDs to assure that the level of awareness of the need for a forceful and targeted research agenda is implemented and that an overall policy on women's health research is implemented trans-NIH. Third, the ORWH and the OMP work together, to implement a strong women and minority policy and projects with individual ICDs and with the ICDs collectively.

The ORWH Research Agenda on Women's Health is the primary goal of the Office of Research on Women's Health. In order to implement this plan efficiently and expeditiously, the Office works directly with the Institutes to establish a forceful and directed agenda on women's health research throughout the National Institutes of Health and extramural community. During FY 1992, the ORWH is directing approximately $7 million toward those diseases and conditions specified in The ORWH Research Agenda on Women's Health. Ongoing meetings have been held with Institute staff to determine the best method for implementing this agenda. Based on those recommendations, a plan has been designed and put in place. This plan requests applications from the Institutes through the following mechanisms:

1) Administrative Supplement -- The ORWH will offer approximately $1.5 million in supplemental funds of up to $50,000 (total costs) per project for FY 1992. These administrative supplements are offered to enable currently funded investigators to: a) enhance targeted research efforts on specific diseases, disorders, or conditions which are described in The ORWH Research Agenda on Women's Health and which affect women's health across the life span; b) enhance the recruitment of women, particularly minority women, within an ongoing study, and/or, c) demonstrate the feasibility of innovative techniques for recruiting or retaining women in research studies.

2) Co-funding. The ORWH will offer approximately $3.5 million in funds of up to $100,000 (total costs) per project for co-funding grants, contracts, or cooperative agreements in FY 1992. These funds are offered to enable investigators to: a) meet the research agenda on specific diseases, disorders, or conditions which are described in The ORWH Research Agenda on Women's Health and which affect women's health across the life span, b) address special projects on topics identified as having special Congressional interest: uterine leiomyomata, endometriosis, HIV and AIDS in women, pelvic inflammatory disease, and sexually transmitted diseases; and c) deliberately expand the study population to include special populations of underserved women (for example, minority women, women in low-income situations, and women in inner cities and rural areas).

3) Special Projects. The ORWH will offer approximately $2 million in funds to Institutes for projects that have been designated by both the ORWH and the Institute as a high priority area for research on women's health. Such areas, already specified in The ORWH Research Agenda on Women's Health, might include, but are not limited to special issues in women's reproductive health, arthritis, immunology, cardiovascular disease and HIV and AIDS in women.

The process of receiving and reviewing the applications for supplementation or co-funding will take place during the spring, with awards expected to be announced no later than the end of June. The Office is currently in the process of identifying representatives of Institutes to serve as reviewers for determining the actual awards.

Mr. Stokes. Because some of your efforts will target minority women, to what extent will you collaborate with minority researchers and minority institutions?

Dr. Pinn. The Office of Research on Women's Health seeks to reach all women across the life span and across all cultures from inner cities to rural counties. In order to accomplish this ambitious and important task, ORWH seeks consultation and counsel from multidisciplinary representatives with expertise in assessing the needs of this diverse population of women. No matter what task is at hand, ORWH exemplifies this diversity in its representatives on task forces and the participants attending workshops, conferences, seminars, and informal consultations. Minority scientists, both women and men, from minority and majority institutions are always present representing not only their academic discipline and specialty, but also sharing their expertise in women's health research or health care delivery. Several examples illustrate this commitment by ORWH.

Women in Biomedical Careers: Dynamics of Change. The Office of Research on Women's Health is keenly aware of the need not only to increase numbers of women in science, but also opportunities for their advancement. To that end, the Office convened a Task Force to gather relevant information on the issues and to hold a Public Hearing and a workshop on the recruitment, retention, re-entry, and advancement of women in biomedical careers. The Task Force is noteworthy because its makeup reflects gender and racial and ethnic diversity. The Task Force is co-chaired by African-American and Hispanic women scientists. The twenty-six member Task Force is composed of 50 percent ethnic and racial minorities representing: African-Americans, Native Americans, Asians, Pacific Islanders, and Hispanic, and 20 percent men.

- The Public Hearing was held March 2-3, 1992, for which nearly 70 organizations provided testimony, with 43 individuals providing oral testimony. Participants traveled from all parts of the United States and were from diverse backgrounds, disciplines, and institutions and organizations. The testimony from this hearing will be used in further developing the agenda for the workshop.

- The workshop, Women in Biomedical Careers: Dynamics for Change, will be held in Bethesda, Maryland on June 11-12, 1992. Approximately 400 participants are expected to attend and will include professionals and those in training across the disciplines and career path: senior scientists, senior academicians (Deans, Chairs), junior faculty, scientific and health professions graduate students, senior level management from professional organizations (for example, the American Medical Association and the American Association of Medical Colleges to the American Women in Science and American Association of University Women), as well as advocates from minority and women's health organizations.

Using the recommendations from the workshop, the ORWH will work closely with the ICDs to design and/or modify and implement training grants and fellowships suited to the needs of women scientists and those in training. Recommendations from this workshop will be published and available upon request to organizations, such as universities, professional schools and organizations, who are in positions to modify or enhance their training and education policies on women in biomedical careers. In addition, ORWH expects that workshop participants, many of whom will represent influential professional organizations, will use the recommendations for action in these organizations and in other arenas.

Recruitment, Retention, and Follow-Up of Women in Research Studies. As the NIH agenda on women's health research goes forward, the issues of recruitment, retention, and follow-up of women in research studies becomes paramount. The difficulties associated with including women encompass not only the medical, legal, and ethical issues, but those related to child care, transportation, and economic hardship. In addition, those women who may be compromised because of poverty, language, or access to medical care, are often not included in studies. Yet, in many instances, these are the women who bear a disproportionate burden of disease morbidity and mortality and whose quality of life is severely impaired. The Office is identifying these issues and defining strategies for addressing them.

The Women's Health Initiative. The Women's Health Initiative, the largest prevention study ever conducted in the United States, will examine the major causes of death, disability and frailty -- heart disease and stroke, breast and colorectal cancer, and osteoporosis -- in older women of all races and socioeconomic strata. Indeed, special attention is being given to recruit and retain minority women in this study for the express purpose of being able to extrapolate study findings to all U.S. women. The study involves ten NIH Institutes and Centers, ensuring that the collective knowledge, expertise, and wisdom will contribute to an integrated, productive research program. Special events include:

- The Concept Review Panel of 10 members for the clinical trial component, convened January 15, 1992, including 2 minorities (African-American and Hispanic) and gave input in the study design such that centers with large minority populations would be eligible.

- The Concept Review Panel for the community randomized trial (CRT) component, convened March 10, 1992, included 6 minorities (3 African-Americans, 1 Native American, 1 Hispanic, 1 Asian/Pacific Islander). These members, along with the others, made recommendations to assure that the construct of this component would facilitate the inclusion of the diverse population of minority women across the country.

- The proposed requirements for selection of CRT community sites include a requirement that, "at least 40 percent of each cross-sectional sample needs to be minority and/or economically disadvantaged to ensure diversity of women."

- The Co-Director of the WHI is an African-American woman, who is also the Director of ORWH. In addition, a representative of the ORWH who has participated in planning meetings is an Hispanic female. Further, the ORWH has identified an African-American woman physician to serve as the ORWH's liaison between the CRT and the Director, ORWH.

- Both the Director of ORWH and the Director of WHI have received "Intent to Apply" inquiries from both minority women scientists and from minority women who wish to participate in the study.

NIH EMPLOYMENT PATTERNS

Mr. Stokes. Dr. Healy, while we applaud the recent placement of minority individuals in several highly visible positions at the NIH, there still is some concern regarding an employment pattern that indicates that there are very few minorities in senior level positions. (Refer to the report they have shared with the office a few weeks ago) What percentage and how many minorities hold managerial positions at the GS-14 level or higher? (Less than 1%)

Dr. Healy. Of the 2,266 managerial positions at NIH in FY 1991, (GS-14 and above) minorities held 251 (11%) of these positions. The following chart provides the number and percentage profile of these positions.

NUMBER AND PERCENT OF MINORITIES IN MANAGERIAL POSITIONS (GS-14 AND ABOVE)

FY 91	TOTAL	NONMINOR.	BLACKS	HISPANICS	ASIANS	AMER. IND.
Number	2,266	2,015	105	33	112	1
Percent	100.0	88.9	4.6	1.5	4.9	0.0

Percentage is based on the total number of managerial positions.

Mr. Stokes. What are the numbers for African Americans?

Dr. Healy. African Americans hold 105 (4.6%) of the 2,266 managerial positions.

Mr. Stokes. To what extent has the total permanent work force increased since 1987? (By about 1,872 or 17%)

Dr. Healy. The NIH total permanent work force increased by 1,872 (+17%) from FY 1987 to FY 1991.

Mr. Stokes. What groups saw the smallest increases?

Dr. Healy. The smallest net increases occurred for Native American men (+3) and women (+8), and Black men (+7).

Mr. Stokes. Which groups was the largest increases?

Dr. Healy. The largest increases occurred for nonminority women (+735) and men (+467).

Mr. Stokes. Provide total numbers and percentages?

Dr. Healy. The following chart provides a comparison of the profiles for FY 1987 and FY 1991 for EEO groups by number and percent based on the permanent work force.

COMPARISON OF TOTAL PERMANENT WORK FORCE FY 87 - FY 91

YEARS	TOTAL	NONMINOR.		BLACK		HISPANIC		ASIAN		AMER. IND.	
		M	W	M	W	M	W	M	W	M	W
FY 87	11052	3348	4715	1061	1452	45	72	136	198	6	17
%	100.0	30.3	42.7	9.6	13.1	0.4	0.7	1.2	1.8	0.0	0.1
FY 91	12924	3815	5450	1068	1809	79	130	219	317	9	25
%	100.0	29.5	42.2	8.3	14.0	0.6	1.0	1.7	2.4	0.0	0.2
DIFFR	1872	467	735	7	357	34	58	83	119	3	8
%*	17.0	13.9	15.6	0.7	24.6	76.0	80.6	61.0	60.1	50.0	47.1

* % - Percentage difference based on each group's FY 87 representation. M = Men, W = Women

In comparison to their representation in the civilian labor force, Hispanics are the most severely underrepresented group in the NIH work force, even though their representation has nearly doubled since FY 1987.

Mr. Stokes. For the record provide a racial/ethnic/sex breakdown per grade level and Institute.

Dr. Healy. Summary statistics of the EEO Group profiles by grade level are provided for each Institute, Center and Division. (The information follows:)

CHARTS

National Cancer Institute
FY 1991
Personnel Employees
Grade Summary Detail #

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	1	0	0	0	0	1	0	0	0	0	0	0
	02	1	0	0	0	0	1	0	0	0	0	0	0
	03	1	1	0	0	0	0	7	2	0	0	0	5
	04	4	2	0	0	0	2	31	11	0	1	0	19
	05	12	5	0	0	0	7	78	29	1	3	0	45
	06	11	3	0	0	0	8	132	41	1	1	0	89
	07	29	12	0	1	0	16	218	60	1	3	1	153
	08	0	0	0	0	0	0	60	7	0	0	0	53
	09	60	22	0	2	0	36	137	15	3	11	1	107
	10	1	0	0	0	0	1	0	0	0	0	0	0
	11	67	9	1	5	1	51	178	10	2	10	0	156
	12	66	9	1	3	0	53	142	10	2	8	0	122
	13	67	5	0	2	0	60	94	6	0	2	1	85
	14	138	2	1	14	0	121	75	9	2	4	0	60
	15	112	1	3	3	0	105	31	3	0	2	0	26
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		570	71	6	30	1	462	1,183	203	12	45	3	920
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	22	0	0	1	0	21	8	0	0	2	0	6
	04	50	2	2	4	0	42	21	2	0	1	0	18
	05	31	1	2	0	0	28	10	1	0	0	0	9
	06	75	0	0	1	0	74	4	0	0	1	0	3
	07	1	0	0	0	0	1	0	0	0	0	0	0
	08	1	0	0	0	0	1	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		180	3	4	6	0	167	43	3	0	4	0	36
TOTAL ES		18	0	0	0	0	18	4	1	0	0	0	3
TOTAL WAGE		6	6	0	0	0	0	2	2	0	0	0	0
ALL OTHER		2	0	0	0	0	2	0	0	0	0	0	0
GRAND TOTAL		776	80	10	36	1	649	1,232	209	12	49	3	959

National Heart, Lung and Blood Institute
FY 1991
Personnel Employees
Grade Summary Detail #

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	2	1	0	0	0	1	0	0	0	0	0	0
	03	2	0	0	0	0	2	3	0	0	0	0	3
	04	1	0	0	0	0	1	4	1	0	0	0	3
	05	13	4	0	1	0	8	29	10	1	2	0	16
	06	8	3	0	1	0	4	36	12	1	2	0	21
	07	9	5	0	0	0	4	101	29	2	2	0	68
	08	5	1	0	0	0	4	30	3	0	1	0	26
	09	24	8	0	1	0	15	44	8	2	3	0	31
	10	6	4	0	0	0	2	4	0	0	0	0	4
	11	23	3	0	2	0	18	51	4	0	3	0	44
	12	15	3	0	0	0	12	47	7	2	2	0	36
	13	23	1	0	0	0	22	33	1	0	1	0	31
	14	52	3	3	6	0	40	34	6	0	1	0	27
	15	42	0	1	2	0	39	12	1	0	2	0	9
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		225	36	4	13	0	172	428	82	8	19	0	319
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	4	2	0	0	0	2	3	0	0	0	0	3
	04	21	0	0	4	0	17	4	1	0	1	0	2
	05	9	1	0	1	0	7	3	0	0	0	0	3
	06	29	0	0	0	0	28	1	0	0	0	0	1
	07	1	0	0	0	0	1	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		64	3	0	5	0	55	11	1	0	1	0	9
TOTAL ES		15	0	0	0	0	15	7	1	0	0	0	6
TOTAL WAGE		4	3	0	0	0	1	6	6	0	0	0	0
ALL OTHER		0	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL		308	42	4	18	0	243	452	90	8	20	0	334

National Library of Medicine
FY 1991
Personnel Employees
Grade Summary Detail #

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	1	0	0	0	0	1	2	1	0	0	0	1
	04	2	2	0	0	0	0	20	11	0	3	0	6
	05	5	2	0	1	0	2	24	10	2	2	0	10
	06	8	4	0	1	0	3	32	8	2	3	0	19
	07	14	9	0	0	0	5	56	20	1	1	0	34
	08	2	1	0	0	0	1	19	9	0	0	0	10
	09	13	3	0	1	0	9	21	6	0	1	1	13
	10	1	1	0	0	0	0	1	0	0	0	0	1
	11	19	4	0	1	0	14	37	6	2	3	0	26
	12	32	6	1	1	0	24	91	8	1	14	0	68
	13	38	3	0	1	0	34	41	2	0	2	0	37
	14	22	0	0	0	0	22	20	2	0	0	0	18
	15	23	2	0	1	0	20	6	0	0	0	0	6
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		180	37	1	7	0	135	370	83	8	29	1	249
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	1	0	0	0	0	1	0	0	0	0	0	0
	05	1	0	0	0	0	1	0	0	0	0	0	0
	06	3	0	0	0	0	3	0	0	0	0	0	0
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		5	0	0	0	0	5	0	0	0	0	0	0
TOTAL ES		5	1	0	0	0	4	1	0	0	0	0	1
TOTAL WAGE		1	0	0	0	0	1	0	0	0	0	0	0
ALL OTHER		0	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL		191	38	1	7	0	145	371	83	8	29	1	250

National Institute for Neurological Disorders and Stroke
FY 1991
Personnel Employees
Grade Summary Detail

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	1	0	0	1	0	0	1	0	0	0	0	1
	03	1	0	0	0	0	1	2	1	0	0	0	1
	04	7	2	0	1	0	4	9	3	0	0	0	6
	05	5	3	0	0	0	2	36	14	2	1	0	19
	06	6	1	0	0	0	5	41	18	0	1	0	22
	07	5	1	0	0	0	4	45	13	2	1	1	28
	08	1	0	0	0	0	1	26	5	0	0	0	21
	09	17	5	0	2	0	10	46	10	1	4	0	31
	10	3	1	0	0	0	2	2	0	0	0	0	2
	11	21	1	1	2	0	17	48	6	0	3	0	39
	12	15	1	0	1	0	13	21	1	0	1	0	19
	13	26	1	0	0	0	25	13	0	0	0	0	13
	14	32	1	1	1	0	29	12	0	0	0	0	12
	15	24	0	0	2	0	22	4	0	0	0	0	4
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		164	17	2	10	0	135	306	71	5	11	1	218
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	3	0	0	0	0	3	5	1	1	0	0	3
	04	8	1	0	0	0	7	3	0	0	0	0	3
	05	7	0	1	0	0	6	1	0	0	0	0	1
	06	19	0	0	1	0	18	0	0	0	0	0	0
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	1	0	0	0	0	1	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		38	1	1	1	0	35	9	1	1	0	0	7
TOTAL ES		14	0	0	0	0	14	0	0	0	0	0	0
TOTAL WAGE		8	3	0	0	0	5	0	0	0	0	0	0
ALL OTHER		0	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL		224	21	3	11	0	189	315	72	6	11	1	225

National Institute of General Medical Sciences
FY 1991
Personnel Employees
Grade Summary Detail #

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	1	0	0	0	0	1
	04	1	0	0	0	0	1	7	3	0	0	0	4
	05	2	1	0	0	0	1	11	5	0	0	0	6
	06	1	0	0	0	0	1	26	8	0	1	0	17
	07	2	1	0	0	0	1	21	5	0	2	0	14
	08	0	0	0	0	0	0	7	3	0	0	0	4
	09	3	1	0	0	0	2	11	3	0	0	0	8
	10	0	0	0	0	0	0	1	0	0	0	0	1
	11	0	0	0	0	0	0	1	0	0	1	0	0
	12	1	0	0	0	0	1	17	2	0	2	0	13
	13	5	1	0	0	0	4	13	1	1	0	0	11
	14	10	1	2	1	0	6	7	1	0	0	0	6
	15	9	2	1	0	0	6	7	1	0	0	0	6
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		34	7	3	1	0	23	130	32	1	6	0	91
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	1	0	0	0	0	1	0	0	0	0	0	0
	04	1	0	0	0	0	1	0	0	0	0	0	0
	05	0	0	0	0	0	0	0	0	0	0	0	0
	06	1	0	0	0	0	1	0	0	0	0	0	0
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		3	0	0	0	0	3	0	0	0	0	0	0
TOTAL ES		2	0	0	0	0	2	4	0	0	0	0	4
TOTAL WAGE		0	0	0	0	0	0	0	0	0	0	0	0
ALL OTHER		0	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL		39	7	3	1	0	282	134	32	1	6	0	95

National Institute of Environmental Health Sciences
FY 1991
Personnel Employees
Grade Summary Detail #

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	6	4	0	0	0	2	12	7	0	0	0	5
	05	6	4	0	1	0	1	23	9	0	0	0	14
	06	3	3	0	0	0	0	41	15	0	0	0	26
	07	13	10	0	0	0	3	49	9	1	0	0	39
	08	2	1	0	0	0	1	8	1	0	0	0	7
	09	38	9	1	0	0	28	48	10	2	1	0	35
	10	1	0	0	0	0	1	1	1	0	0	0	0
	11	24	3	0	1	0	20	36	4	0	3	0	29
	12	18	2	0	1	0	15	26	5	0	0	0	21
	13	37	3	0	1	0	33	11	2	0	0	0	9
	14	44	0	0	2	0	42	11	1	0	0	0	10
	15	33	0	1	3	0	29	2	0	0	0	0	2
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		225	39	2	9	0	175	268	64	3	4	0	197
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	3	0	0	0	0	3	2	0	0	0	0	2
	05	4	0	0	0	0	4	0	0	0	0	0	0
	06	7	0	0	0	0	7	0	0	0	0	0	0
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		14	0	0	0	0	14	2	0	0	0	0	2
TOTAL ES		10	1	0	0	0	9	1	0	0	0	0	1
TOTAL WAGE		35	15	0	0	0	20	1	0	0	0	0	1
ALL OTHER		1	0	0	0	0	1	0	0	0	0	0	0
GRAND TOTAL		285	55	2	9	0	219	272	64	3	4	0	201

National Institute of Dental Research
FY 1991
Personnel Employees
Grade Summary Detail

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	1	0	0	0	0	1
	03	1	0	0	1	0	0	0	0	0	0	0	0
	04	3	1	0	0	0	2	13	3	0	1	0	9
	05	1	0	0	0	0	1	9	3	1	0	0	5
	06	1	1	0	0	0	0	11	4	0	0	0	7
	07	3	2	0	0	0	1	24	6	0	0	0	18
	08	0	0	0	0	0	0	11	4	0	0	1	6
	09	6	2	0	0	0	4	14	2	2	2	0	8
	10	0	0	0	0	0	0	0	0	0	0	0	0
	11	8	2	1	0	0	5	17	0	0	1	0	16
	12	5	0	0	0	0	5	18	0	1	0	0	17
	13	13	0	0	2	0	11	11	1	0	2	0	8
	14	13	1	0	1	0	11	12	1	0	0	0	11
	15	17	0	1	0	0	16	7	1	0	0	0	6
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		71	9	2	4	0	56	148	25	4	6	1	112
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	4	3	0	0	0	1	0	0	0	0	0	0
	04	1	0	0	0	0	1	0	0	0	0	0	0
	05	3	1	0	0	0	2	0	0	0	0	0	0
	06	14	0	0	1	0	13	1	0	0	0	0	1
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		22	4	0	1	0	17	1	0	0	0	0	1
TOTAL ES		3	0	0	0	0	3	1	0	0	0	0	1
TOTAL WAGE		6	5	0	0	0	1	1	0	0	0	0	1
ALL OTHER		0	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL		102	18	2	5	0	77	151	25	4	6	1	115

National Institute of Diabetes and Diagnostic and Kidney Diseases
FY 1991
Personnel Employees
Grade Summary Detail #

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	1	0	1	0	0	0	5	2	0	0	0	3
	05	3	1	0	0	0	2	11	7	0	0	0	4
	06	3	1	0	0	0	2	30	8	0	1	0	21
	07	3	2	0	1	0	0	45	13	1	0	1	30
	08	0	0	0	0	0	0	23	4	0	0	1	18
	09	11	5	0	1	0	5	17	3	0	2	0	12
	10	0	0	0	0	0	0	1	0	0	0	0	1
	11	9	1	0	0	0	8	34	5	2	4	0	23
	12	17	1	0	1	0	15	20	5	0	1	0	14
	13	15	2	0	1	0	12	14	2	0	0	0	12
	14	37	2	2	2	0	31	16	1	0	2	0	13
	15	40	0	0	2	0	38	9	0	0	0	0	9
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		139	15	3	8	0	113	225	50	3	10	2	160
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	1	0	0	0	0	1	1	0	0	0	0	1
	04	13	1	1	2	0	9	2	0	0	0	0	2
	05	3	2	0	0	0	1	0	0	0	0	0	0
	06	21	2	0	0	0	19	2	0	1	0	0	1
	07	1	0	0	0	0	1	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		39	5	1	2	0	31	5	0	1	0	0	4
TOTAL ES		21	0	0	0	0	21	1	0	0	0	0	1
TOTAL WAGE		3	2	0	0	0	1	4	4	0	0	0	0
ALL OTHER		0	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL		202	22	4	10	0	166	235	54	4	10	2	165

National Institute of Deafness and Other Communication Disorders
FY 1991
Personnel Employees
Grade Summary Detail

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	1	0	0	0	0	1	0	0	0	0	0	0
	04	1	1	0	0	0	0	1	1	0	0	0	0
	05	0	0	0	0	0	0	6	4	0	0	0	2
	06	1	1	0	0	0	0	10	4	1	1	0	4
	07	0	0	0	0	0	0	17	5	0	2	0	10
	08	0	0	0	0	0	0	3	1	0	0	0	2
	09	1	0	1	0	0	0	7	3	0	0	0	4
	10	0	0	0	0	0	0	1	1	0	0	0	0
	11	1	0	0	0	0	1	6	1	0	1	0	4
	12	3	0	0	0	0	3	9	1	0	0	0	8
	13	3	0	0	0	0	3	7	1	0	0	0	6
	14	2	0	0	0	0	2	7	0	0	0	0	7
	15	1	0	0	0	0	1	3	0	0	0	0	3
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		14	2	1	0	0	11	77	22	1	4	0	50
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	0	0	0	0	0	0	0	0	0	0	0	0
	05	0	0	0	0	0	0	0	0	0	0	0	0
	06	0	0	0	0	0	0	0	0	0	0	0	0
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		0	0	0	0	0	0	0	0	0	0	0	0
TOTAL ES		4	0	0	0	0	4	0	0	0	0	0	0
TOTAL WAGE		0	0	0	0	0	0	0	0	0	0	0	0
ALL OTHER		0	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL		18	2	1	0	0	15	77	22	1	4	0	50

National Institute of Child Health and Human Development
FY 1991
Personnel Employees
Grade Summary Detail #

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	2	0	0	1	0	1	1	0	1	0	0	0
	03	0	0	0	0	0	0	2	1	0	1	0	0
	04	3	1	0	0	0	2	8	1	0	1	0	6
	05	3	0	0	1	0	2	13	4	0	0	0	9
	06	4	2	0	0	0	2	18	7	0	1	0	10
	07	5	1	1	0	0	3	52	11	0	0	0	41
	08	0	0	0	0	0	0	17	1	0	1	0	15
	09	4	1	0	0	0	3	18	2	0	1	0	15
	10	0	0	0	0	0	0	2	1	0	0	0	1
	11	8	2	1	0	0	5	24	2	0	3	0	19
	12	13	1	0	1	0	11	33	7	0	2	0	24
	13	12	1	0	0	0	11	13	0	0	2	0	11
	14	29	1	1	7	0	20	16	1	0	0	0	15
	15	21	0	0	2	0	19	10	0	0	3	0	7
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		104	10	3	12	0	79	227	38	1	15	0	173
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	1	0	0	0	0	1	1	0	0	1	0	0
	04	16	1	0	0	0	15	8	0	0	0	0	8
	05	1	0	0	0	0	1	2	1	0	0	0	1
	06	17	0	0	3	0	14	0	0	0	0	0	0
	07	1	0	0	0	0	1	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		36	1	0	3	0	32	11	1	0	1	0	9
TOTAL ES		10	0	0	0	0	10	2	0	0	0	0	2
TOTAL WAGE		0	0	0	0	0	0	2	2	0	0	0	0
ALL OTHER		1	0	0	0	0	1	0	0	0	0	0	0
GRAND TOTAL		151	11	3	15	0	122	242	41	1	16	0	184

National Institute of Arthritis and Musculoskeletal Diseases
FY 1991
Personnel Employees
Grade Summary Detail #

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	1	0	0	0	0	1	5	3	0	0	0	2
	05	1	0	0	0	0	1	4	1	0	1	0	2
	06	1	1	0	0	0	0	5	2	0	0	0	3
	07	1	0	0	0	0	1	19	5	0	1	0	13
	08	0	0	0	0	0	0	3	1	0	0	0	2
	09	0	0	0	0	0	0	10	2	0	0	0	8
	10	0	0	0	0	0	0	1	0	0	0	0	1
	11	4	0	0	1	0	3	0	0	0	0	0	0
	12	2	1	0	0	0	1	10	0	0	0	1	9
	13	1	0	0	0	0	1	6	0	0	2	0	4
	14	5	0	0	0	0	5	8	0	0	0	0	8
	15	11	1	0	1	0	9	1	0	0	0	0	1
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		27	3	0	2	0	22	72	14	0	4	1	53
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	1	0	0	0	0	1	2	0	0	0	0	2
	04	0	0	0	0	0	0	3	0	0	0	0	3
	05	1	0	0	0	0	1	0	0	0	0	0	0
	06	7	0	0	0	0	7	0	0	0	0	0	0
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		9	0	0	0	0	9	5	0	0	0	0	5
TOTAL ES		4	0	0	0	0	4	0	0	0	0	0	0
TOTAL WAGE		1	1	0	0	0	0	0	0	0	0	0	0
ALL OTHER		0	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL		41	4	0	2	0	35	77	14	0	4	1	58

National Institute of Allergy and Infectious Diseases
FY 1991
Personnel Employees
Grade Summary Detail #

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	3	0	1	0	0	2
	03	1	1	0	0	0	0	0	0	0	0	0	0
	04	6	2	2	0	0	2	10	7	0	0	0	3
	05	8	4	1	0	0	3	29	17	0	2	0	10
	06	9	6	0	0	0	3	49	14	0	1	0	34
	07	13	2	0	2	0	9	68	16	0	3	0	49
	08	0	0	0	0	0	0	22	3	0	1	0	18
	09	33	4	0	3	0	26	52	7	1	4	1	39
	10	0	0	0	0	0	0	2	0	0	0	0	2
	11	46	10	1	1	0	34	77	6	2	9	0	60
	12	20	3	0	1	0	16	62	5	0	3	0	54
	13	29	1	0	0	0	28	43	5	2	1	0	35
	14	43	3	0	4	0	36	38	3	3	2	0	30
	15	36	2	0	1	0	33	19	0	1	1	0	17
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		244	38	4	12	0	190	474	83	10	27	1	353
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	5	0	0	0	0	5	2	0	0	0	0	2
	04	16	1	0	0	0	15	11	4	0	2	0	5
	05	5	0	0	0	0	5	1	0	0	0	0	1
	06	36	0	0	0	0	36	0	0	0	0	0	0
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	1	0	0	0	0	1	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		63	1	0	0	0	62	14	4	0	2	0	8
TOTAL ES		15	0	0	0	0	15	1	0	0	1	0	0
TOTAL WAGE		24	4	0	0	0	20	3	0	0	0	1	2
ALL OTHER		3	0	0	0	0	3	0	0	0	0	0	0
GRAND TOTAL		349	43	4	12	0	290	492	87	10	30	2	363

National Institute on Aging
FY 1991
Personnel Employees
Grade Summary Detail #

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	1	0	1	0	0	0	1	0	0	1	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	3	1	0	0	0	2	5	2	0	1	0	2
	05	5	1	0	2	0	2	16	6	0	0	0	10
	06	2	1	0	0	0	1	34	9	0	2	0	23
	07	2	2	0	0	0	0	26	6	0	0	0	20
	08	0	0	0	0	0	0	7	1	0	0	0	6
	09	5	0	0	0	0	5	21	5	0	0	0	16
	10	0	0	0	0	0	0	0	0	0	0	0	0
	11	13	1	0	1	0	11	35	2	2	2	0	29
	12	8	0	0	0	0	8	27	2	1	0	0	24
	13	21	0	0	1	0	20	13	1	0	0	0	12
	14	21	0	0	1	0	20	9	0	0	1	0	8
	15	18	0	1	0	0	17	6	1	0	0	0	5
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		99	6	2	5	0	86	200	35	3	7	0	155
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	3	0	0	0	0	3	1	0	0	0	0	1
	05	2	0	1	0	0	1	0	0	0	0	0	0
	06	16	0	0	0	0	16	0	0	0	0	0	0
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		21	0	1	0	0	20	1	0	0	0	0	1
TOTAL ES		7	0	0	0	0	7	2	0	0	0	0	2
TOTAL WAGE		19	14	0	0	0	5	7	5	0	0	0	2
ALL OTHER		0	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL		146	20	3	5	0	118	210	40	3	7	0	160

National Eye Institute
FY 1991
Personnel Employees
Grade Summary Detail

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	1	1	0	0	0	0
	03	0	0	0	0	0	0	1	0	0	0	0	1
	04	0	0	0	0	0	0	2	1	0	0	0	1
	05	1	1	0	0	0	0	1	0	0	0	0	1
	06	0	0	0	0	0	0	8	4	0	0	0	4
	07	2	0	0	0	0	2	23	4	0	0	1	18
	08	0	0	0	0	0	0	7	4	0	0	0	3
	09	6	3	0	0	0	3	13	1	1	1	0	10
	10	0	0	0	0	0	0	0	0	0	0	0	0
	11	4	1	0	0	0	3	14	3	0	1	0	10
	12	7	2	0	0	0	5	10	1	1	2	0	6
	13	6	0	0	0	0	6	10	2	1	1	0	6
	14	12	0	0	2	1	9	9	1	0	0	0	8
	15	14	1	0	0	0	13	6	0	0	0	0	6
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		52	8	0	2	1	41	105	22	3	5	1	74
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	2	1	0	0	0	1	0	0	0	0	0	0
	05	0	0	0	0	0	0	0	0	0	0	0	0
	06	3	0	0	0	0	3	0	0	0	0	0	0
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		5	1	0	0	0	4	0	0	0	0	0	0
TOTAL ES		7	0	0	0	0	7	0	0	0	0	0	0
TOTAL WAGE		1	1	0	0	0	0	0	0	0	0	0	0
ALL OTHER		1	0	0	0	0	1	0	0	0	0	0	0
GRAND TOTAL		66	10	0	2	1	53	105	22	3	5	1	74

National Center for Research Resources
FY 1991
Personnel Employees
Grade Summary Detail #

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	1	1	0	0	0	0	0	0	0	0	0	0
	03	1	1	0	0	0	0	0	0	0	0	0	0
	04	5	1	1	0	0	3	14	5	1	1	0	7
	05	5	2	0	0	0	3	16	8	0	1	0	7
	06	5	3	0	0	0	2	27	9	0	0	0	18
	07	6	4	0	0	0	2	37	8	1	1	0	27
	08	1	0	0	1	0	0	7	2	0	0	0	5
	09	3	2	0	0	0	1	16	2	0	1	0	13
	10	0	0	0	0	0	0	1	0	0	0	0	1
	11	27	4	0	1	0	22	23	8	0	0	0	15
	12	14	3	0	1	0	10	25	5	0	0	0	20
	13	11	4	0	0	0	7	16	5	0	2	0	9
	14	23	2	1	0	0	20	7	2	0	0	0	5
	15	9	1	0	0	0	8	5	0	0	0	0	5
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		111	28	2	3	0	78	194	54	2	6	0	132
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	0	0	0	0	0	0	1	0	0	0	0	1
	05	1	0	0	0	0	1	1	0	0	0	0	1
	06	8	2	0	0	0	6	1	0	0	0	0	1
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	1	0	0	0	0	1	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		10	2	0	0	0	8	3	0	0	0	0	3
TOTAL ES		1	0	0	0	0	1	1	0	0	0	0	1
TOTAL WAGE		35	7	0	2	0	26	1	0	0	0	0	1
ALL OTHER		0	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL		157	37	2	5	0	113	199	54	2	6	0	137

National Center for Nursing Resources
FY 1991
Personnel Employees
Grade Summary Detail

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	0	0	0	0	0	0	0	0	0	0	0	0
	05	0	0	0	0	0	0	2	1	0	0	0	1
	06	0	0	0	0	0	0	5	2	0	1	0	2
	07	1	0	0	0	0	1	4	2	0	0	0	2
	08	0	0	0	0	0	0	1	0	0	0	0	1
	09	0	0	0	0	0	0	1	0	0	0	0	1
	10	0	0	0	0	0	0	1	0	0	0	0	1
	11	0	0	0	0	0	0	0	0	0	0	0	0
	12	0	0	0	0	0	0	8	1	0	0	0	7
	13	0	0	0	0	0	0	3	0	0	0	0	3
	14	1	0	0	1	0	0	4	0	0	0	0	4
	15	1	0	0	0	0	1	5	1	0	0	0	4
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		3	0	0	1	0	2	34	7	0	1	0	26
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	0	0	0	0	0	0	1	0	0	0	0	1
	05	0	0	0	0	0	0	1	0	0	0	0	1
	06	0	0	0	0	0	0	1	0	0	0	0	1
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		0	0	0	0	0	0	3	0	0	0	0	3
TOTAL ES		0	0	0	0	0	0	1	0	0	0	0	1
TOTAL WAGE		0	0	0	0	0	0	0	0	0	0	0	0
ALL OTHER		0	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL		3	0	0	1	0	2	38	7	0	1	0	30

National Center for Human Genome Research
FY 1991
Personnel Employees
Grade Summary Detail #

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	0	0	0	0	0	0	0	0	0	0	0	0
	05	1	1	0	0	0	0	2	2	0	0	0	0
	06	0	0	0	0	0	0	2	2	0	0	0	0
	07	1	0	0	1	0	0	10	5	0	0	0	5
	08	0	0	0	0	0	0	1	0	0	0	0	1
	09	0	0	0	0	0	0	2	1	0	0	0	1
	10	0	0	0	0	0	0	0	0	0	0	0	0
	11	0	0	0	0	0	0	2	0	0	0	0	2
	12	1	0	1	0	0	0	2	2	0	0	0	0
	13	0	0	0	0	0	0	3	0	0	0	0	3
	14	0	0	0	0	0	0	4	1	0	0	0	3
	15	4	0	0	0	0	4	3	1	0	0	0	2
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		7	1	1	1	0	4	31	14	0	0	0	17
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	0	0	0	0	0	0	0	0	0	0	0	0
	05	0	0	0	0	0	0	0	0	0	0	0	0
	06	0	0	0	0	0	0	0	0	0	0	0	0
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		0	0	0	0	0	0	0	0	0	0	0	0
TOTAL ES		0	0	0	0	0	0	1	0	0	0	0	1
TOTAL WAGE		0	0	0	0	0	0	0	0	0	0	0	0
ALL OTHER		0	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL		7	1	1	1	0	4	32	14	0	0	0	18

Fogarty International Center
FY 1991
Personnel Employees
Grade Summary Detail #

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	2	0	0	0	0	2	2	0	0	0	0	2
	05	2	0	0	0	0	2	11	2	2	1	0	6
	06	0	0	0	0	0	0	7	1	0	0	0	6
	07	0	0	0	0	0	0	6	1	0	0	0	5
	08	0	0	0	0	0	0	2	0	0	0	0	2
	09	1	0	0	1	0	0	3	0	0	0	0	3
	10	0	0	0	0	0	0	1	0	0	0	0	1
	11	0	0	0	0	0	0	3	0	0	0	0	3
	12	0	0	0	0	0	0	4	0	0	0	0	4
	13	0	0	0	0	0	0	2	0	0	0	0	2
	14	5	1	0	0	0	4	4	0	0	0	0	4
	15	8	0	0	0	0	8	2	0	0	0	0	2
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		18	1	0	1	0	16	47	4	2	1	0	40
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	0	0	0	0	0	0	0	0	0	0	0	0
	05	0	0	0	0	0	0	0	0	0	0	0	0
	06	2	0	0	1	0	1	0	0	0	0	0	0
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		2	0	0	1	0	1	0	0	0	0	0	0
TOTAL ES		1	0	0	0	0	1	0	0	0	0	0	0
TOTAL WAGE		0	0	0	0	0	0	0	0	0	0	0	0
ALL OTHER		0	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL		21	1	0	2	0	18	47	4	2	1	0	40

Office of the Director
FY 1991
Personnel Employees
Grade Summary Detail #

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	1	0	0	0	0	1	1	0	0	0	0	1
	03	0	0	0	0	0	0	1	1	0	0	0	0
	04	21	15	0	1	0	5	31	17	0	0	1	13
	05	14	7	0	0	0	7	51	27	1	2	0	21
	06	15	6	1	0	0	8	55	31	1	3	0	20
	07	15	8	0	0	0	7	107	34	2	2	0	69
	08	1	1	0	0	0	0	46	17	0	0	1	28
	09	17	10	0	0	0	7	54	11	1	1	1	40
	10	0	0	0	0	0	0	7	0	0	0	0	7
	11	19	6	0	1	0	12	48	12	0	0	1	35
	12	41	10	1	1	0	29	86	16	1	2	0	67
	13	57	11	2	4	0	40	85	14	0	2	0	69
	14	53	6	1	0	0	46	34	5	0	0	0	29
	15	33	1	2	0	0	30	16	1	0	0	0	15
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		287	81	7	7	0	192	622	186	6	12	4	414
CC	01	0	0	0	0	0	0	0	0	0	0	0	0
	02	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	0	0	0	0	0
	04	0	0	0	0	0	0	1	1	0	0	0	0
	05	3	0	0	0	0	3	0	0	0	0	0	0
	06	11	1	0	0	0	10	1	0	0	1	0	0
	07	0	0	0	0	0	0	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		14	1	0	0	0	13	2	1	0	1	0	0
TOTAL ES		17	3	0	1	0	13	1	0	0	0	0	1
TOTAL WAGE		71	58	0	0	0	13	1	1	0	0	0	0
ALL OTHER		1	0	0	0	0	1	0	0	0	0	0	0
GRAND TOTAL		390	143	7	8	0	232	626	188	6	13	4	415

Central Services
FY 1991
Personnel Employees
Grade Summary Detail

		MALES						FEMALES					
		TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN	TOTAL	BLACK	HISPN	ASIAN	AMER. INDIAN	NON MIN
GS/GM	01	1	0	0	0	0	1	0	0	0	0	0	0
	02	1	1	0	0	0	0	6	5	0	0	0	1
	03	8	3	0	2	0	3	28	14	1	1	1	11
	04	66	30	2	5	0	29	109	61	2	3	1	42
	05	125	57	4	6	1	57	201	111	3	4	1	82
	06	52	28	1	2	0	21	163	79	6	7	1	70
	07	64	31	1	5	0	27	225	77	7	5	0	136
	08	32	13	0	2	0	17	86	29	0	2	0	55
	09	74	22	0	3	0	49	266	46	6	19	0	195
	10	18	2	0	0	0	16	416	29	10	20	2	355
	11	94	17	6	3	0	68	280	35	8	16	1	220
	12	106	21	0	3	0	82	196	22	5	3	1	165
	13	131	9	4	13	0	105	72	8	2	4	0	58
	14	146	10	2	14	0	120	44	0	0	4	0	40
	15	53	2	1	2	0	48	18	2	0	1	0	15
	16	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL GS/GM		971	246	21	60	1	643	2,110	518	50	89	8	1,445
CC	01	0	0	0	0	0	0	8	2	0	0	0	6
	02	2	0	0	0	0	2	20	1	0	1	0	18
	03	2	0	0	0	0	2	26	3	1	2	1	19
	04	21	0	2	2	0	17	31	4	0	1	0	26
	05	35	1	0	0	0	34	28	2	0	0	0	26
	06	42	1	0	1	0	40	12	1	0	1	0	10
	07	1	0	0	0	0	1	0	0	0	0	0	0
	08	0	0	0	0	0	0	0	0	0	0	0	0
	09	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL CC		103	2	2	3	0	96	125	13	1	5	1	105
TOTAL ES		8	0	0	0	0	8	0	0	0	0	0	0
TOTAL WAGE		556	230	6	6	6	308	149	139	4	0	0	6
ALL OTHER		1	0	0	0	0	1	0	0	0	0	0	0
GRAND TOTAL		1,639	478	29	69	7	1,056	2,384	670	55	94	9	1,556

Mr. Stokes. Information shared with my office indicates that in terms of the total workforce profile there has been very little change in the minority profile since 1987. In fact, the participation rate for black males has dropped by 2%. What factors are contributing to this decline?

Dr. Healy. We have not identified a specific cause for the decline in the employment of Black men at NIH. However, the statistics over the past 5 years indicate that there is more of a problem with retention since the separation rate for Black men has increased, while our record of hiring Black men is comparable to the hiring of the other EEO protected groups.

Mr. Stokes. What are you doing to address this issue?

Dr. Healy. We are still in the process of identifying factors that affect this issue. Most ICDs have established exit interviews to obtain information from separating employees, and the remaining ICDs are being encouraged to implement this process. The NIH Black Employees Advisory Committee plans to review all separation actions for FY 1992 to determine reasons for separations and will make recommendations to change any NIH policies that are barriers to the retention of Black men, as well as other minorities. In addition, we are continuing to expand recruitment for minorities by strengthening our Federal Equal Opportunity Recruitment Program (FEORP) and holding ICD Directors responsible for approving selections for all FEORP targeted positions. The NIH Black Employment Program Manager has established a Minority Recruitment Network with over 200 contacts that will be available to ICD Personnel Offices seeking to reach minority applicants.

Mr. Stokes. Regarding these imbalances, how do you plan to address these imbalances in the future? Also, for the record, would you provide a list of those minority individuals who administer programs with budgets over which they have some discretion.

Dr. Healy. In addition to the emphasis on exit interviews, and expanded targeted recruitment, we are in the process of implementing two mechanisms to hold managers and supervisors accountable for the EEO posture of their organizations. In FY 1992 we will initiate on-site reviews of each ICD's EEO programs, including the Affirmative Employment Programs for Minorities, Women, and the Disabled, FEORP, and the EEO Complaints Program. Beginning in FY 1993, we will also implement an EEO critical performance element for all managers and supervisors. By having a specific element on EEO and an evaluation mechanism in place, all managers and supervisors will be held accountable and rated on their recruitment and retention of minorities, women, and people with disabilities.

We do not, at the present, have in place a system for tracking minorities in positions with budgetary discretion. However, because of the tremendous impact and high visibility we are aware of the following organizations whose leaders are minorities with budgetary discretion.

Director, Office of Extramural Programs	(Black man)
Acting Director, Office of Research on Women's Health	(Black woman)
Director, National Institute of Environmental Health Sciences	(Black man)
Director, Office of Minority Programs	(Black man)
Director, Office of Equal Opportunity	(Black woman)
Chief, Office of Scientific Review	(Black woman)
Director, Office of Financial Management	(Black man)
Director, Division Space Management	(Black man)
Director, Division of Engineering Services	(Hispanic man)
Director, Minority ACCESS to Research Careers Program Branch	(Black man)
Director, Biomedical Research Support Program Branch	(Hispanic man)
Director, Research Centers in Minority Institutions Program	(Black man)
Director, Division of Extramural Activities, NCI	(Black woman)
Director, Housekeeping and Fabric Care Department, CC	(Black man)
Chief, Materials Management Department, CC	(Black man)

Mr. Stokes. How many minorities are in tenured positions or in positions of similar professional autonomy by ICD and race or ethnic background. Provide similar data regarding the number of minorities serving on advisory councils. Break the information down by race or ethnic background.

Dr. Healy. Summary statistics of the EEO Group profiles are provided for each Institute, Center and Division. (The information follows:)

FY 91 PROFILE OF NIH TENURED POSITIONS
BY RACE/ETHNIC GROUP
SENIOR EXECUTIVE SERVICE

ICD	TOTAL	NONMIN.	BLACKS	HISPANICS	ASIANS	AMER. INDIANS
OD	18	14	3	0	1	0
ORS	1	1	0	0	0	0
NIA	9	9	0	0	0	0
NIAID	16	15	0	0	1	3
NIAMS	4	4	0	0	0	0
NCI	22	21	1	0	0	0
NICHD	12	12	0	0	0	0
NIDCD	4	4	0	0	0	0
NIDR	4	4	0	0	0	0
NIDDK	22	22	0	0	0	0
NEI	7	7	0	0	0	0
NIEHS	11	10	1	0	0	0
NIGMS	6	6	0	0	0	0
NHLBI	22	21	1	0	0	0
NCHGR	1	1	0	0	0	0
NINDS	14	14	0	0	0	0
NCNR	1	1	0	0	0	0
NCRR	2	2	0	0	0	0
FIC	1	1	0	0	0	0
NLM	6	5	1	0	0	0
CC	2	2	0	0	0	0
DCRT	3	3	0	0	0	0
DRG	2	2	0	0	0	0
TOTAL	190	181	7	0	2	0
%		95.3	3.7	0.0	1.0	0.0

FY 91 PROFILE OF NIH TENURED POSITIONS
BY RACE/ETHNIC GROUP
COMMISSIONED CORPS LEVEL 06 AND ABOVE

ICD	TOTAL	NONMIN.	BLACKS	HISPANICS	ASIANS	AMER. INDIANS
OD	12	10	1	0	1	0
ORS	9	8	1	0	0	0
NIA	16	16	0	0	0	0
NIAID	37	37	0	0	0	0
NIAMS	7	7	0	0	0	0
NCI	81	79	0	0	2	0
NICHD	18	15	0	0	3	0
NIDCD	0	0	0	0	0	0
NIDR	15	14	0	0	1	0
NIDDK	24	21	2	1	0	0
NEI	3	3	0	0	0	0
NIEHS	7	7	0	0	0	0
NIGMS	1	1	0	0	0	0
NHLBI	30	30	0	0	0	0
NCHGR	0	0	0	0	0	0
NINDS	20	19	0	0	1	0
NCNR	0	0	0	0	0	0
NCRR	10	8	2	0	0	0
FIC	2	1	0	0	1	0
NLM	3	3	0	0	0	0
CC	35	32	1	0	2	0
DCRT	4	4	0	0	0	0
DRG	7	7	0	0	0	0
TOTAL	341	322	7	1	11	0
%		94.4	2.0	0.3	3.2	0.0

FY 91 PROFILE OF NIH TENURED POSITIONS
BY RACE/ETHNIC GROUP
GS/GM - 13, 14, 15 LEVELS

ICD	TOTAL	NONMIN.	BLACKS	HISPANICS	ASIANS	AMER. INDIANS
OD	278	229	38	5	6	0
ORS	119	89	9	7	14	0
NIA	88	82	2	1	3	0
NIAID	208	179	14	6	9	0
NIAMS	32	28	1	0	3	0
NCI	517	457	26	6	27	1
NICHD	101	83	3	1	14	0
NIDCD	23	22	1	0	0	0
NIDR	73	63	4	1	5	0
NIDDK	131	115	7	2	7	0
NEI	57	48	4	1	3	1
NIEHS	138	125	6	1	6	0
NIGMS	51	39	7	4	1	0
NHLBI	196	168	12	4	12	0
NCHGR	14	12	2	0	0	0
NINDS	111	105	2	1	3	0
NCNR	14	12	1	0	1	0
NCRR	71	54	14	1	2	0
FIC	21	20	1	0	0	0
NLM	150	137	9	0	4	0
CC	82	70	6	1	5	0
DCRT	105	100	4	0	1	0
DRG	158	127	12	1	18	0
TOTAL	2,738	2,364	185	43	144	2
%		86.3	6.8	1.6	5.2	0.0

FY 91 PROFILE OF NIH TENURED POSITIONS
BY RACE/ETHNIC GROUP
GS 9-12 LEVELS

ICD	TOTAL	NONMIN.	BLACKS	HISPANICS	ASIANS	AMER. INDIANS
OD	272	197	65	3	5	2
ORS	164	104	56	2	2	0
NIA	109	93	10	3	3	0
NIAID	292	231	35	4	21	1
NIAMS	27	22	3	0	1	1
NCI	651	526	75	9	39	2
NICHD	102	78	16	1	7	0
NIDCD	28	20	6	1	1	0
NIDR	68	55	6	4	3	0
NIDDK	109	78	20	2	9	0
NEI	54	37	11	2	4	0
NIEHS	192	149	34	3	6	0
NIGMS	34	25	6	0	3	0
NHLBI	214	162	37	4	11	0
NCHGR	7	3	3	1	0	0
NINDS	173	133	25	2	13	0
NCNR	10	9	1	0	0	0
NCRR	109	82	24	0	3	0
FIC	12	11	0	0	1	0
NLM	215	155	34	4	21	1
CC	1,112	909	113	31	55	4
DCRT	105	87	12	1	5	0
DRG	69	50	13	1	5	0
TOTAL	4,128	3,216	605	78	218	11
%		77.9	14.7	1.9	5.3	0.3

FY 91 PROFILE OF NIH TENURED POSITIONS
BY RACE/ETHNIC GROUP
COMMISSIONED CORPS LEVEL 01-05

ICD	TOTAL	NONMIN.	BLACKS	HISPANICS	ASIANS	AMER. INDIANS
OD	4	3	1	0	0	0
ORS	16	16	0	0	0	0
NIA	6	5	0	1	0	0
NIAID	40	33	5	0	2	0
NIAMS	7	7	0	0	0	0
NCI	142	124	6	4	8	0
NICHD	29	26	2	0	1	0
NIDCD	0	0	0	0	0	0
NIDR	8	4	4	0	0	0
NIDDK	20	14	3	1	2	0
NEI	2	1	1	0	0	0
NIEHS	9	9	0	0	0	0
NIGMS	2	2	0	0	0	0
NHLBI	44	34	4	0	6	0
NCHGR	0	0	0	0	0	0
NINDS	27	23	2	2	0	0
NCNR	3	3	0	0	0	0
NCRR	3	3	0	0	0	0
FIC	0	0	0	0	0	0
NLM	2	2	0	0	0	0
CC	154	131	13	3	6	1
DCRT	2	2	0	0	0	0
DRG	1	1	0	0	0	0
TOTAL	521	443	41	11	25	1
%		85.0	7.9	2.1	4.8	0.2

FY 91 PROFILE OF NIH ADVISORY COMMITTEE/CONSULTANTS BY RACE/ETHNIC GROUP

ICD	TOTAL	NONMIN.	BLACKS	HISPANICS	ASIANS	AMER. INDIANS
OD	91	80	2	4	5	0
ORS	2	1	0	1	0	0
NIA	33	29	4	0	0	0
NIAID	67	58	5	1	3	0
NIAMS	38	36	0	1	1	0
NCI	134	115	4	5	10	0
NICHD	56	48	4	2	2	0
NIDCD	59	47	3	3	6	0
NIDR	41	34	2	3	2	0
NIDDK	110	94	6	5	4	1
NEI	26	20	4	1	1	0
NIEHS	81	68	7	2	4	0
NIGMS	14	9	2	2	1	0
NHLBI	118	90	17	7	4	0
NCHGR	24	22	1	0	1	0
NINDS	45	39	2	2	2	0
NCNR	18	15	2	0	1	0
NCRR	26	19	5	1	1	0
FIC	11	8	2	0	1	0
NLM	45	37	4	2	2	0
CC	5	4	0	0	1	0
DCRT	0	0	0	0	0	0
DRG	7	6	1	0	0	0
TOTAL	1,051	879	77	42	52	1
PERCENT	100.0	83.6	7.3	4.0	5.0	0.1

GROOMING YOUNGER MINORITIES

Mr. Stokes. I am concerned that there seems to be no training ground or career development focus for minority individuals at NIH. When I talk to minority representatives of NIH, they are usually long-term employees. Seldom do I have any contact with younger or newer employees who give the impression that they are in a career ladder or are being groomed for advancement into senior level positions. Can you tell us what steps you have taken to assure the infusion, development and retention of young people, particularly minorities, who might eventually be chosen for senior positions in the NIH scientific or administrative workforce?

Dr. Healy. NIH has a number of initiatives underway aimed at providing career opportunities, development and retention of young people. The initiatives address training of employees for internal placement in senior level vacancies, improving the work environment, and developing a pipeline for future employment of minorities at NIH. Specifically, the initiatives are: The Executive Development Program, which is a developmental program that will provide specific training to minorities and women to create a pool of highly qualified minorities and women for priority placement in vacancies for senior level positions; EEO Training for Managers and

Supervisors, which has a curriculum under development to assure uniform training of managers and supervisors on the basic EEO policies and regulations, managing culturally diverse work environments and EEO complaints processing; and the Minority Science Career Orientation Program that is designed to provide minority high school students with technical work experience and communication in a scientific environment to challenge and create an interest in biomedical research careers at NIH. In addition, many ICDs have established "Adopt-a-School" programs wherein they support area public high schools with substantial minority enrollments, by supplementing their science programs, targeting summer employment opportunities for students, and assisting teachers in improving the science curriculum for students to foster more interest in biomedical research. The targeted schools include D.C.'s McKinley and Dunbar High Schools, both of which have majority Black students.

TRAINING GRANTS

Mr. Stokes. In March of 1986, the National Institutes of Health published a policy regarding the recruitment of minority individuals into NIH National Research Service Awards, specifically into institutional training grants. At that time, the representation of minorities on NIH training grants was abysmally low. Can you tell us what steps have been taken, first to facilitate, then to enforce, the effective implementation of this policy?

Dr. Healy. Several of the ICDs have promoted minority recruitment by publishing minority locators to assist research training directors in making contact with directors of Minority Access to Research Career (MARC) and Minority Biomedical Research Support (MBRS) grants. The Research Training and Special Programs Office has also budgeted money to develop an NIH-wide locator in FY 1992.

At this point, virtually all training grant applications include a plan to recruit minority trainees and most are considered adequate by initial review groups. In all cases, however, the administrative note in the summary statement and the plan in the application are carefully considered by program staff prior to award. Over the period from FY 1989 to 1991, NIH ICDs have reported approximately 30 applications which required an improved minority recruitment plan prior to award.

Mr. Stokes. Would you please provide this Committee, for the record, data that would show what has happened at NIH over the past several years with regard to minority recruitment on these grants?

Dr. Healy. The NIH has no definitive information on the number of minority trainees in NRSA programs, for reasons stated above. Since receiving permission from OMB to collect relevant information, we have inserted questions about race/ethnicity into the Statement of Appointment Form (PHS 2271) which is to be completed by all trainees at the time of each appointment or reappointment. By February, 1993 we expect to have collected a full year of information on the distribution of traineeships to the various ethnic categories.

PROCESSING OF COMPLAINTS

Mr. Stokes. Information shared with my office indicates that NIH is taking longer to process EEO complaints. In 1989, the agency held on to these complaints for 228 days. For FY 1991, days totaled 445. Why is it taking longer for NIH to process these complaints?

Dr. Healy. The prime reason for the increased processing time is the increase in the numbers of complaints being filed. In FY 90, the NIH received 135 informal complaints; in FY 91, we received 194; and so far, just 6 months into the FY 92, we have received 136. In order to respond to the increase in the number of complaints, we are expanding the number of collateral-duty EEO Counselors. So far this year, we have increased the number from 23 to 53 and project at least 22 more for total of 75 by the end of FY 92. In FY 91 our resolution rate of effectively solving complaints was 66%. With an expanded staff of counselors, we expect to significantly reduce the processing time for complaints and concomitantly increase the resolution rate at the informal level.

Mr. Stokes. Furthermore, while there has been an increase in the number of complaints received since 1989 (from 19 to 35), you are processing fewer (from 19 to 2). Why?

Dr. Healy. NIH began FY 89 with a large backlog of complaints which had been investigated and were awaiting preparation of Proposed Dispositions. A major effort was undertaken to prepare the Proposed Dispositions and eliminate the backlog. Hence the record shows a fairly high number of cases processed in FY 89 compared to FY 91. Further, as the number of inquiries and informal complaints increased, the emphasis shifted to early intervention at the informal level. As previously mentioned, our resolution rate for FY 91 was 66%.

Mr. Stokes. How do current staffing levels in the EEO office compare to the 1989 levels?

Dr. Healy. The Office of Equal Opportunity is currently staffed with 23 full-time positions as compared to 17 in 1989.

OFFICE OF RESEARCH ON WOMEN'S HEALTH

Mr. Early. Since you received a significant increase over the budget request for the ORWH, would you summarize your program plans for FY 92?

Dr. Healy. The Office of Research on Women's Health (ORWH) addresses a three-fold mandate: 1) to strengthen and enhance research related to diseases and conditions that affect women, and 2) to ensure that research conducted and supported by NIH adequately addresses issues regarding women's health and that women are appropriately represented in biomedical and biobehavioral research studies supported by the NIH, and 3) that opportunities are presented and supported for recruitment, retention, re-entry, and advancement of women in biomedical careers.

To address the primary goal of this three-fold mandate in FY 1992, the ORWH is directing approximately $7 million toward those diseases and conditions specified in The ORWH Research Agenda on Women's Health: $5 million in administrative supplements and co-funding and $2 million for special high priority projects such as an 1992 RFA, co-funded by the ORWH and the National Institute of Child Health and Human Development, addressing state of the art fibroid and endometriosis research of clinical importance. To date, several meetings have been held with ICD staff to determine the best method for implementing this agenda. Based on those recommendations a mechanism for action has been designed and will be in place by March 25, 1992. This plan requests applications from the ICDs for funding research on women's health in the following ways:

1. Administrative Supplement. The ORWH will offer approximately $1.5 million in supplemental funds of up to $50,000 (total costs) per project for FY 1992. These administrative supplements are offered to enable currently funded investigators to: a) enhance targeted research efforts on specific diseases, disorders, or conditions which are described in The ORWH Research Agenda on Women's Health and which affect women's health across the life span; b) enhance the recruitment of women, particularly minority women, within an ongoing study, and/or, c) demonstrate the feasibility of innovative techniques for recruiting or retaining women in research studies.

2. Co-funding. The ORWH will offer approximately $3.5 million in funds of up to $100,000 (total costs) per project for co-funding, with the Institutes and Centers, grants, contracts, or cooperative agreements of investigators with new proposals in FY 1992. These funds are offered to enable investigators to: a) meet the research agenda on specific diseases, disorders, or conditions which are described in The ORWH Research Agenda on Women's Health and which affect women's health across the life span, b) address special projects on topics identified as having special Congressional interest: uterine leiomyomata, endometriosis, HIV and AIDS in women, pelvic inflammatory disease, and sexually

transmitted diseases; and c) deliberately expand the study population to include special populations of underserved women (for example, minority women, women in low-income situations, women in inner cities and rural areas).

3. Special Projects. The ORWH will offer approximately $2 million in amounts to be determined by the ORWH and the particular Institute for projects that have been designated by both the ORWH and that particular Institute as a high priority area for research on women's health. Such projects, already specified in The ORWH Research Agenda on Women's Health, might include, but are not limited to special issues in women's reproductive health, arthritis, immunology, cardiovascular disease and HIV and AIDS in women.

The process of receiving and reviewing the applications for supplementation or co-funding will take place during the spring with awards expected to be announced no later than the end of June. The Office is currently in the process of identifying representatives of Institutes to serve as reviewers for determining the actual awards.

The remaining constraint is the current limitation of funding to 1 year for the ORWH. The ability to offer funding for larger than a one year period will be necessary to support and encourage broader initiatives.

In addition to implementing the research agenda, Dr. Vivian Pinn, Director, ORWH, is the Co-director of the **Women's Health Initiative**, the largest prevention study ever conducted in the United States, will examine the major causes of death, disability and frailty -- heart disease and stroke, breast and colorectal cancer, and osteoporosis -- in older women of all races and socioeconomic strata. The study involves ten NIH Institutes and Centers, ensuring that the collective knowledge, expertise, and wisdom will contribute to an integrated, productive research program. The requests for applications to become a center for this trial are about to be released. Upon the awards to the centers, probably in early fall 1992, the study will commence.

In addition to implementing the research agenda, the Office is actively engaged in a series of additional activities supporting the other two goals of the three-fold mandate:

1. To ensure that research conducted and supported by NIH adequately addresses issues regarding women's health and that women are appropriately represented in biomedical and biobehavioral research studies supported by the NIH. The Office, in cooperation with the Office of Minority Programs and the Office of Extramural Research, has taken steps to implement a strengthened trans-NIH policy on the inclusion of women in biomedical and biobehavioral studies. The responsibility for monitoring this process and tracking the inclusion of women in NIH-supported research now rests with the Office. A series of actions have been implemented to

ensure that the policy will be maintained and the strengthened guidelines have been monitored closely in the first years of operation and are being revised based upon the responses from Initial Review Groups, NIH Scientific Review Administrators, and NIH Advisory Councils.

2. To ensure opportunities are presented and supported for recruitment, retention, re-entry, and advancement of women in biomedical careers.

The Office of Research on Women's Health is, thus, keenly aware of the need not only to increase numbers of women in science, but also opportunities for their advancement. To that end, the Office convened a Task Force to gather relevant information on the issues and to hold a Public Hearing and a workshop on the recruitment, retention, re-entry, and advancement of women in biomedical careers. The Task Force is noteworthy because its makeup reflects gender and racial and ethnic diversity. The Task Force is co-chaired by an African-American and an Hispanic woman scientist. The twenty-six member Task Force is composed of 50 percent ethnic and racial minorities representing: African-Americans, Native American, Asians, Pacific Islanders, and Hispanics, as well as 20 percent men.

In addition to the Task Force deliberations, the Office held a Public Hearing to invite interested organizations to present testimony on the subject. The Public Hearing was held March 2-3, 1992, for which nearly 70 organizations provided testimony, with 43 individuals providing oral testimony. Participants traveled from all parts of the United States and were from diverse backgrounds, disciplines, and institutions and organizations.

Recommendations from the Task Force deliberations and the Public hearing testimony are being folded into plans for the workshop, **Women in Biomedical Careers: Dynamics of Change**, to be held June 11-12 1992 in Bethesda, Maryland. This workshop expects the deliberations to recommend ways to enhance recruitment, retention, and promotion of women in science.

Mr. Early. In general, how did you determine the purposes for which these additional resources would be used?

Dr. Healy. In the first year of operation, ORWH established the basis for the research agenda on women's health and in the second year designed and is implementing that agenda: The ORWH Research Agenda on Women's Health. The third year will see a more refined and targeted research agenda.

This agenda is based on the recommendations from the ORWH Public Hearing and Workshop, Opportunities for Research on Women's Health (September 1991), the Scientific Initiative -- Women, Minorities, and the Underserved -- contained within the NIH Planning Document, as well as the many consultations and discussions from scientific and clinical experts and the lay public.

The primary source for the decision in how to utilize these additional resources most effectively came from the ORWH workshop on Opportunities for Research on Women's Health. This workshop was designed to identify scientific research opportunities and gaps in knowledge and to recommend a comprehensive trans-NIH plan for future directions for research on women's health. In order to prepare for that workshop the Task Force, convened to direct design and plan the workshop, held a Public Hearing which brought together the viewpoints of the more than 90 women's health advocates groups spanning the health interest spectrum, from Sjogren's Syndrome to breast cancer and heart disease, to recommend an NIH research agenda on women's health.

These efforts culminated in a scientific workshop, **Opportunities for Research on Women's Health** September 4-6, 1991, to recommend a trans-NIH research agenda for the next decade. Over 300 culturally diverse scientists, ethicists, attorneys, educators, and women's health advocates attended. Workshop participants focused on biomedical and biobehavioral issues in two major areas: across the life span and special diseases and conditions. The Workshop Proceedings will be available in June 1992.

The ORWH Research Agenda on Women's Health, a direct result of the workshop and planning with the ICDs during the NIH Strategic Plan activities, directs research efforts aimed at promoting and enhancing health and preventing and/or controlling disease among women across the life span, from before birth to old age. The agenda will be accomplished through research efforts encompassing biomedical and biobehavioral research spectrum from basic science through clinical trials to community demonstration and education studies. Diseases or conditions that have not had sufficient research attention (for example, coronary heart disease, AIDS, menopause) or diseases or conditions among certain groups of women (such as minority groups or underserved) which have not received sufficient research attention (for example, systemic lupus erythematosus, diabetes, osteoporosis) will be addressed. In addition, attention to those diseases and conditions of interest to Congress will be addressed: uterine fibroids, endometriosis, pelvic inflammatory disease, relationship between oral contraceptive use and breast cancer, women and AIDS, and the status and on-going health effects of those exposed to the synthetic estrogen drug DES.

The monies from the Office to the ICDs are intended to supplement research activities on women's health research and not to replace monies that would not ordinarily be spent on such activities.

Mr. Early. What portion of your resources will be used to augment new initiatives, and how much will be used to expand current studies?

Dr. Healy. Approximately $5.5 million will be used to augment new initiatives and approximately $1.5 million will be used to expand current studies for a total of $7 million. The remainder of the $10.240 million is being used for program support, training opportunities for women scientists, and for the support of workshops, **Women in Biomedical Careers -- Dynamics of Change**, and other ICD workshops, such as the NICHD workshop, **Abnormal Uterine Bleeding, Myomas, and Infertility**, the NCI workshops, **Long-term Health Effects of Exposure to Diethylstilbestrol (DES)**, and **Occupational Cancers and Women**, as well as the NIAMS sponsored workshop on **The Female Athlete: Amenorrhea, Eating Disorders, and Osteoporosis**.

Mr. Early. Doctor, would you highlight for us the recommendations of the workshop on "Opportunities for Research on Women's Health"?

Dr. Healy. To achieve its mandate on an trans-NIH research agenda, the Office held a public hearing in which over 60 organizations interested in women's health testified on a women's health research agenda at NIH. An additional 30 organizations responded in writing.

The recommendations from the public hearing were folded into the design of the ORWH workshop, Opportunities for Research on Women's Health. This workshop addressed critical gaps in knowledge and considered methods to enhance on-going work in women's health research and presented recommendations for action -- across the life span and within specific disease entities. Participants included over 300 culturally diverse scientists, clinical researchers, ethicists, economists, clinicians, and women's health advocates considered gaps in research on women's health and made recommendations for such an agenda at the NIH for the next several decades.

The recommendations for research included the following two major areas with the specific call for action within each:

RESEARCH ACROSS THE LIFE SPAN

- Birth to Young Adulthood (Birth to 24 years): Because mortality is low in this group, key research interest will revolve around injuries and risk-taking behavior which are the major threats rather than disability and disease: better understanding of biologic differences between males and females; elucidate patterns of normal development among females including understanding that society is not gender neutral; understanding how lifelong patterns begun and maintained which affect later health such as health-promoting and health-risking behavior; societal and individual views on bodies which leads to eating disorders, obesity, depression, and suicide; and, adaptation to pregnancy and motherhood.

- Young Adulthood to Perimenopausal Years (15-45): In this area, research efforts will consider sexually transmitted diseases, reproductive morbidity (pregnancy-related, contraception, infertility), psychosocial morbidity, injuries, malignancies, and cardiovascular diseases. As always, there is a critical need to place the research within the context of societal and individual factors across all cultural and socioeconomic groups.

- Perimenopausal to Mature Years (45-64). This is the age when menopause occurs and chronic conditions manifest themselves which affect life span and quality of life. This is also one of the least researched areas in women's health research. Menopause has received relatively little attention in research and thus requires efforts directed toward population-based, clinical, and lab approaches. Three priority areas have been identified: understanding effects of estrogen on health, understanding effects of behavior on health, and understanding the differences in health status among socioeconomic, race and ethnic groups.

- Mature Years (65+). While these women (the "old-old") are survivors, their quality of life is often severely compromised due to co-morbid conditions, frailty, dementia, and lack of care-givers. These areas require considerably more attention.

RESEARCH ON DISEASES AND CONDITIONS

Research efforts will also focus on specific diseases and conditions:

- Reproductive Biology. Areas for a research focus on brain and reproductive function, ovarian functions and their control, term and pre-term labor, uterine dysfunction, hormones and behavior, control of mammary gland growth and development. Clearly this area also relates strongly to the ages birth to perimenopausal years described above.

- Early Developmental Biology. The primary research initiatives in this particular area would include those which would optimize pregnancy outcome and provide understanding of the basic science foundations of normal embryonic development in relation to clinical problems. Such efforts might encompass model systems (including such efforts as molecular genetics, targeted mutagenesis) and genetic variation.

- Cardiovascular Function and Diseases. Coronary Heart Disease, in particular, has not received the attention in the scientific and medical community that is warranted considering the magnitude of the problem among women. Therefore, this must be a priority research area. Six priority areas were identified as requiring considerably greater attention: sex hormones, psychosocial factors, diabetes mellitus, physical exercise, hypertension, obesity, thrombosis, and the relationship of racial and ethnic biology and socio-economic factors. The research portfolio should encompass the full biomedical and biobehavioral research spectrum from basic research including genetics through epidemiological, prevention clinical trials.

- **Malignancies**. This area requires extensive investigation with special attention to women who are poor or who have limited access to care. Specific attention must be directed toward cancers of the breast, ovaries and uterus, colorectal, and lung. As with the Cardiovascular area, the cancer research portfolio should encompass the full biomedical and biobehavioral research spectrum from basic research including genetics through epidemiological, prevention clinical trials.

- **Immune and Infectious Diseases**. Among the immune diseases, certain disease are aberrations of the immune system which seem to affect women in disproportionate numbers such as Grave's Disease, Hashimoto's Disease, Rheumatoid Arthritis, Systemic Lupus Erythematosus, and Scleroderma. These diseases have not always had the attention nor the resources necessary to elucidate their pathology and/or treatment. The research activities should include: basic research (etiology, pathogenesis, new disease models), epidemiology/natural history, clinical intervention, and behavioral/educational strategies. Among the infectious diseases, the primary emphasis should be on sexually transmitted diseases and the HIV virus.

- **Aging**. The research focus in this area, closely related to the above described section on the "Mature" years, includes four general strategies: define mechanisms (cellular or subcellular, organ, regulatory) by which comorbidity causes physical disability with aging; determine interactions of co-morbid conditions: final common pathways of disability; establish methods to measure severity of co-morbid conditions; and, seek to understand the decline in homeostatic reserves that occur with aging and lead to fatality.

The proceedings are being prepared and will be available in summer 1992.

Mr. Early. How do these recommendations fit into the overall NIH Strategic Plan?

Dr. Healy. The Office, in cooperation with the Office of Minority Programs (OMP), co-chaired a section of the plan, Women, Minorities, and the Underserved. The NIH ICDs participated fully in the development of this section contributing their specific recommendations for research dedicated to women's health. Their recommendations for action are remarkably congruent with the recommendations from the workshop, **Opportunities for Research on Women's Health**. As such the recommendations from both have been blended into the Office research plan for action, **The ORWH Research Agenda on Women's Health**.

Mr. Early. I understand that ORWH was able to provide some supplemental funding in FY 91 for current grants. For what areas of research did you provide support?

Dr. Healy. The ORWH provided over $800,000 in supplemental funds for on-going research grants at the NIH. Of the 41 grants received for supplemental funding, half were awarded. Of those, half of the investigators were women. The research funded ranged from efforts to reduce adolescent tobacco use to determinants of the onset of myocardial infarction.

Mr. Early. Would you briefly summarize your program plans and priorities for FY 93?

Dr. Healy. **The ORWH Research Agenda on Women's Health** is an ambitious undertaking that will require several years to bring to complete fruition. In the first year of operation, ORWH established the basis for the research agenda on women's health and in the second year designed and is implementing that agenda: The ORWH Research Agenda on Women's Health. The third year will see a more refined and targeted research agenda.

During this third year, and beyond, ORWH, in cooperation with the ICDs, will seek to develop more fully many of the recommendations contained in The ORWH Research Agenda on Women's Health. The ORWH plans to consider health issues within each phase of the life span and to develop research protocols that address some of the most pressing issues. In the phase, Birth to Early Adulthood, the Office might focus attention on the risk taking behaviors of young women, e.g., eating disorders, sexually transmitted diseases or other behaviors such as smoking that set the stage for chronic diseases in later life. In the phase, Young Adulthood to Perimenopausal Years, the Office might focus on issues surrounding reproductive morbidity (fertility control and contraception, infertility, medically-assisted conception, endometriosis, pregnancy loss, fetal health, uterine leiomyomata, and pelvic inflammatory disease). In the phase, Perimenopausal to Mature Years, the Office might focus on issues pertaining to the overall health profile of women and the risk of serious disease, including molecular mechanisms that lead to the decline of ovarian function; basic and clinical studies of hormone replacement therapy; effect of behavior, socioeconomic status, racial and ethnic differences on health status; and identification of women at high risk for cardiovascular disease.

Clearly the agenda is, and should be, an ambitious one. It must, however, continue to be developed in concert with the ICDs for, ultimately, this agenda must become an integral part of each NIH ICD.

The Office will continue monitoring and evaluating the Tracking System on the Inclusion of Women and Minorities as well as continuing to provide education on the system for Internal Review Groups, Advisory Councils, and NIH program staff.

As part of refining this research agenda and monitoring the inclusion of women in clinical studies, the Office will also address concerns surrounding the recruitment, retention, and follow-up of women in clinical studies. This issue is a pervasive one that requires considerable attention if we are to understand how to accomplish these factors expeditiously and effectively.

The Office will continue to pursue training and educational support opportunities for women scientists and those considering careers in science.

Mr. Early. Doctor, would you tell us what kind of education and outreach activities the office currently supports and whether you are planning any new initiatives?

Dr. Healy. The Office is keenly aware of the need to apprise not only the scientific community of its existence and mandate, but the lay public, with its private organizations and entrepreneurs, as well. Indeed, the activities of speaking, counselling, and serving as members of advisory groups, which have been undertaken by the very small staff of professionals (2 scientists and 1 lawyer-nurse) to date have been extensive. Indeed, the Office has been received with enthusiasm in each place it has been and has generated more interest and action in women's health and women's health research. We are gratified to learn of the level of interest and research already underway across the country from the small women's colleges and Historically Black Colleges and Universities to the large institutions and medical centers. Powerful and culturally diverse women's organizations have offered their expertise in recruiting women for clinical studies. The media calls daily for interviews and information. Our Office, however, cannot begin to meet the requirements for advice, consultation, speaking, keynote addresses, radio and TV appearances, other media interview, with such a small staff and restricted travel budget.

Responding to such requests and preparing speeches and written communications currently consumes an inordinate amount of our office time and energy. However, we recognize the value of this outreach and we are making every effort to meet public expectations as well as our own expectations of what is necessary. To that end, the Office is in the process of hiring staff, not only to assist in education and outreach, but for the myriad other tasks an office of this scope requires. In addition to hiring at least two more scientists, one a physician, we are in the process of hiring a Public Affairs Officer who can work extensively with the media, prepare office-related materials and coordinate those from other ICDs for use with private and public organizations, and prepare and staff an Office exhibit at seminars and conferences across the country.

To extend our reach, the Office has formed a subcommittee within The Advisory Committee on Women's Health Issues (ACWHI), an advisory committee to the Director, ORWH. This Subcommittee on ORWH Speaker's Roster devises a list of qualified speakers and prepares materials for them to use in fulfilling the numerous speaking engagement requests that come into the ORWH. The subcommittee further maintains a list of the speaking engagements and evaluations prepared by the speakers upon return from the presentation. In addition, the ACWHI also maintains a Subcommittee on the Women's Health and Behavior Seminar Series. This group is preparing a series of seminars for presentation at NIH on women's health issues. The seminar series presented by this group last year was quite successful and has been in demand again this year.

Because we believe that education and outreach are essential to our operation, we will be developing new education and outreach initiatives in this arena in three major areas: information about ORWH and its mandate and activities, **The ORWH Research Agenda on Women's Health**, and in training and fellowships for women scientists.

Sending information on the hundreds of requests for Office descriptions as well as information from other Institutes, other key issues in women's health that may or may not be readily available (and thus require time and effort to acquire), for radio and television interviews as well as maintaining a data bank on information and individuals requires staff and time resources.

SHANNON AWARDS

Mr. Early. Doctor, how much are you planning to allocate for "Shannon Awards" in FY 92 and FY 93?

Dr. Healy. We are currently reviewing the success rate for R01 awards as well as ways in which my FY 1992 discretionary funds can best be used. The Shannon Awards are a priority and we plan to fund as many as possible in FY 1992 and FY 1993. In FY 1992, we will not be able to use the $15 million used from my transfer authority as was done in FY 1991, because the Shannon Award initiative does not meet the "Emergency" criteria placed on the FY 1992 transfer fund authority.

Mr. Early. How many "Shannon Awards" were made last year?

Dr. Healy. In FY 1991, 310 Shannon Awards were made.

Mr. Early. Would you provide for the record a table displaying, by Institute, the number of Shannon awards?

Dr. Healy. A table displaying the number of Shannon Awards made by Institutes and Centers follows:

FY 91 Shannon Awards

Number of Awards	Institutes and Center
15	National Institute on Aging (NIA)
32	National Institute of Allergy and Infectious Diseases (NIAID)
11	National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
55	National Cancer Institute (NCI)
5	National Institute on Deafness and Other Communication Disorders (NIDCD)
4	National Institute of Dental Research (NIDR)
34	National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
6	National Institute of Environmental Health Sciences (NIEHS)
13	National Eye Institute (NEI)
43	National Institute of General Medical Sciences (NIGMS)

22	National Institute of Child Health and Human Development (NICHD)
4	National Center for Human Genome Research (NCHGR)
27	National Heart, Lung, and Blood Institute (NHLBI)
5	National Center for Nursing Research (NCNR)
30	National Institute of Neurological Disorders and Stroke (NINDS)
4	National Center for Research Resources (NCRR)
310	

SENIOR BIOMEDICAL RESEARCH SERVICE PROGRAM

Mr. Early. What is the status of the Senior Biomedical Research Service Program?

Dr. Healy. Final issues are currently being discussed within the Administration. Once there is resolution and the regulation is approved, PHS/NIH Personnel instructions will be completed and appointments effected.

Mr. Early. How many slots has NIH requested, and how many have you received?

Dr. Healy. NIH expects to receive 235 (67%) of the total 350 legislated slots with the opportunity to compete with other participating PHS agencies for a pool of 30 slots retained by the Assistant Secretary for Health.

Mr. Early. How do you plan to allocate these slots among the Institutes?

Dr. Healy. NIH will allocate SBRS slots based on the scientific merit of the individuals nominated. Based on a PHS/SBRS Policy Board prescribed nomination procedure, the Director, NIH, will distribute up to 95% of the total NIH allocation to Institutes, Divisions, and Centers (ICDs) to recruit outside scientists and to retain outstanding NIH researchers. A small number of slots (5%) will be held in a Director's reserve to accommodate any unforeseen needs. Once an individual leaves the SBRS, the slot will revert back to the Director's reserve. ICD Directors may request allocations from this reserve to fill new or vacated positions.

EXTRAMURAL FACILITIES

Mr. Early. The FY 92 bill included $7.5 million for extramural facilities construction grants. What are your plans in this area?

Dr. Healy. On January 31 of this year we published in the NIH Guide for Grants and Contracts a Request for Applications for institutions and organizations to seek funds for construction of research facilities. Applicants may request up to 50 percent of the allowable costs of a project, not to exceed $2 million. Based on the receipt of 92 letters-of-intent, to date, we anticipate that approximately 65 applications will be submitted by the receipt date of April 27. Initial peer review will be conducted in mid-July, with secondary review by the relevant National Advisory Council or

Board in early September, and final funding decisions to be made before the end of September. We anticipate making 4 to 5 awards.

Mr. Early. Doctor, what is your assessment of the need for a general authority for extramural facilities construction and funds?

Dr. Healy. Based on information we have obtained from a survey conducted under the auspices of the NIH and the National Science Foundation in 1990 we believe that research facility construction is needed by the biomedical science disciplines supported by all of the NIH Institutes and Centers. The greatest need, however, as identified in the June 1990 "Report on Biomedical Research Facilities Construction" is with minority institutions. The panel recommended that as funds become available these needs should be addressed first. In concert with these recommendations we have proposed a $12 million initiative in FY 1993. An authorizing legislation will be submitted shortly.

WOMEN'S HEALTH INITIATIVE

Mr. Early. Doctor, how are you utilizing the $25 million provided to initiate the Women's Health Study?

Dr. Healy. The $24.8 million for the first year of the Women's Health Initiative will be utilized as follows. The bulk of the money, $23.5 million, will be awarded as contracts to 16 groups in the United States. These 16 contracts will fund 1 coordinating center and 15 clinical centers for the Clinical Trial/ Observational Study. About 4% of the $24.8 million or $0.8 million will be expended for administrative costs, such as staff salaries, consultations, peer review, and site visits before awarding contracts.

Mr. Early. For FY 93, you have requested $44.5 million. How will these funds be allocated among the three components of this study?

Dr. Healy. The $44.5 million request for FY 93 will be allocated as follows (in thousands):

Clinical trial/observational study	$33,000
Community study	$10,000
Administrative costs	$ 1,500

The clinical trial and observational study components have been merged into a one component to increase scientific and financial efficiency.

Mr. Early. What process will be used to select the coordinating center and the 50 clinical centers for the clinical trial and observational study?

Dr. Healy. The same process will be used to review and select the coordinating center and 50 clinical centers as that used by all NIH institutes in contracting. The initial technical evaluation by non-NIH scientists and the second stage technical evaluation is by

NIH scientists. The proposals will be peer reviewed by panels of non-NIH scientists selected for their expertise.

Mr. Early. Will there be a mix of existing study section members, or will a new peer review panel be established?

Dr. Healy. The peer review groups will be separate panels but will contain many members of advisory groups and study sections from various institutes. There will be separate initial technical review panels for the coordinating center and the clinical centers. Because of the extensive interest in applying for the clinical centers we anticipate that most knowledgeable and capable potential reviewers will be applicants. To avoid the obvious conflict of interest that might result, we have developed a plan that would avoid a conflict of interest but preserve our ability to use the best and most capable reviewers. The applications from the eastern United States could be reviewed by scientists from the western states and, in a separate review, applications from the western states could be reviewed by eastern scientists. Following this peer review the proposals in the competitive range will be evaluated further. NIH will conduct a technical evaluation including aspects of business and negotiation. Site visits by NIH staff to competitive institutions will be performed and negotiations completed before final discussions are made.

Mr. Early. What is the timetable for the selection/award process?

Dr. Healy. The timetable for the selection/award process for the Clinical Trial/Observational Study coordinating center and clinical center is as follows:

Coordinating Center:

March 17, 1992	RFP issued
May 15, 1992	RFP closed
July 13, 1992	Initial technical evaluation completed
August 1992	NIH review and negotiation
September 30, 1992	Contracts awarded

Clinical Centers:

April 13, 1992	RFP issued
June 12, 1992	RFP closed
August 7, 1992	Initial technical evaluation completed
September 1992	NIH review and negotiation
September 30, 1992	Contracts awarded

Mr. Early. Which Institutes are involved in this phase of the study?

Dr. Healy. The following Institutes and Centers are participating currently in the Women's Health Initiative:

The National Cancer Institute
National Heart, Lung and Blood Institute
National Institute on Aging

National Institute of Arthritis, Musculoskeletal and Skin Diseases
National Institute of Child Health and Human Development
National Center for Nursing Research
National Institute of Diabetes, Digestive and Kidney Diseases
National Institute for Dental Research

The Office of Disease Prevention and Office of Research on Women's Health, Office of the Director are coordinating the study.

Mr. Early. Will they be allocating funds to these component studies?

Dr. Healy. Principal funding for the Women's Health Initiative will come from the Office of the Director, NIH. Institutes may choose to allocate additional funds to support related research involving the Women's Health Initiative and are encouraged to do so.

Mr. Early. Doctor, will any of the participants of the "Framingham Heart Study" be involved in this program?

Dr. Healy. The awards to clinical centers have not been made; therefore, it is not possible to know whether a clinical center would be in proximity to Framingham, Massachusetts. If a clinical center were accessible to Framingham women, those who are 50 to 79 years of age would be eligible for the study regardless of their participation in the "Framingham Heart Study."

FINANCIAL MANAGEMENT PLAN

Mr. Early. Are, or will, recent advances, such as molecular biology and structural biology, affect the cost of doing research?

Dr. Healy. Many projects in areas such as molecular biology and structural biology require an initial expensive outlay for the high technology instrumentation that is required. Much of this instrumentation can be shared not only regionally but even nationally. Thus, not every investigator needs an array of sophisticated equipment in his/her own laboratory to conduct these kinds of projects, and therefore the overall cost should not be significantly increased.

Mr. Early. Will the increased use of computers and parallel processing affect cost?

Dr. Healy. In the case of super-computers and parallel processors, again, a similar situation applies. These expensive pieces of equipment can be shared by many investigators across the country and their speed of operation should off-set the man-hours currently required.

Mr. Early. Do you expect that we will see more multi-disciplinary projects?

Dr. Healy. It is most likely we will see an increase in multidisciplinary projects. This is so because of the sophistication of the equipment required, the array of technologies involved and the need for broad expertise to be brought together to answer questions we are asking at the molecular and cellular level in modern biology and medicine.

Mr. Early. Are these more expensive?

Dr. Healy. Many of these projects will be more costly than our current average research project grants. However, these multidisciplinary projects will be composed of collaborative individual projects, reducing the number of total projects with, in many cases, a reduction in cost because of the collaboration.

Mr. Early. Do epidemiology projects, such as those searching for biomarkers, tend to be more expensive?

Dr. Healy. Epidemiology studies are generally considered to be more costly than those involving basic research utilizing cellular or in vitro laboratory applications. These studies involve the use of specific population segments that must be identified, enrolled, interviewed, tested and tracked. The human risk factor inherent in these studies would also be a factor relating to increased cost.

Mr. Early. Doctor, do we need to adjust the current average level of support for research project grants?

Dr. Healy. At this time NIH is operating in accordance with the provisions of the Financial Management Plan submitted to Congress in June 1991. Thus we are allowing the average cost of competing grants to increase from year to year by no more than the Biomedical Research and Development Price Index (BRDPI). We believe that we are able to achieve this objective and are closely monitoring and adjusting our award levels to ensure adherence to the BRDPI. As we gain experience from this process, we will keep the Committee informed of any unanticipated concerns or issues that may arise with respect to the average cost of research project grants.

Mr. Early. Do we need to allow for the fact that some types of projects, such as clinical trials and epidemiology studies, tend to be more expensive?

Dr. Healy. Clinical trials, epidemiology studies and other population based studies are generally more costly. On the other hand, some behavioral studies are less expensive. The former is due to a number of factors: follow-up of large numbers of patients (sometimes in the tens of thousands) for several years; coordination and involvement of multiple centers and sites; labor-intensive nature of these efforts; large volume of data to be collected and analyzed; special laboratory studies; and assurance of quality control throughout the project.

For all these reasons, population based studies can be and usually are more expensive than the traditional research project. When these more costly studies are aggregated with the regular research grants, they can significantly affect the average cost of awards for any given Institute that supports several of these studies. The opposite can hold true for an institute with a portfolio intensive in behavioral research.

Mr. Early. Doctor, have there been any problems with the amount of increase allowed for a competing grant over preceding noncompeting status?

Dr. Healy. Because the annual increase in the average cost of competing research project grants may not exceed the Biomedical Research and Development Price Index (BRDPI), when competing continuation awards are made by NIH, one of the factors used in determining the appropriate award amount is the level of support provided in the preceding non-competing budget year. Consideration of this factor allows us to provide some degree of growth while exercising prudent management of overall costs.

Of course, in limiting the growth of competing continuation grants, some elements of the proposed research may necessarily have to be curtailed or postponed. This may result in investigators' submitting new grant applications for that portion of the proposed research that was not funded. If this were to occur, NIH would experience in the near future an increase in the number of grant applications submitted for funding. Such an increase would naturally have consequences for the workload of our review groups, and would skew data on success rates.

In some cases, because of the size of the increase provided in the competing continuation awards, we are unable to allow the investigator to pursue his/her research as aggressively or as rapidly as proposed.

Mr. Early. Doctor, do we have a good idea of the cost of doing research? I hear that we don't and that more information and data need to be collected before we really have a good idea of the cost.

Dr. Healy. The information we have on the cost of research is focused at the project level of support and it is based largely on the costs that NIH awards, not what may actually be required to conduct the research. We do not know, for example, the true costs of establishing or supporting a laboratory effort in a particular field of science, in part because the total array of the laboratory's support both institutional and Federal, is not apparent to us. We do not know the amount of institutional support for direct or indirect costs that is over and above the specific project support provided by NIH.

We intend to conduct some specific studies in this area. One has already begun under the auspices of the Office of Management and Budget and the Office of Science Technology and Policy, with the collaboration of the Association of American Universities and the Council on Governmental Relations. This study, which began primarily because of the allocated overhead problem, will shed more light on the actual level of institutional expenditures for direct and overhead costs. Additionally, NIH will conduct other studies to specify the actual costs of the conduct of certain research projects, not just the NIH contribution. All these studies will help us over time to determine the proper level of NIH funding in the context of all sources of support.

TRAVEL REDUCTION

Mr. Early. Doctor, what impact are the travel reductions having on the programs under your office?

Dr. Healy. The travel reductions impact several of our programs in turns of their outreach and educational objectives and affect our oversight responsibilities. For example, site visits to conduct investigations of scientific misconduct and audits of research and development contractors and NIH grantees are being curtailed. Travel related to the recruitment of post-doctoral fellows and students in residency will be decreased. Further participation of NIH's senior staff and policy administrators in significant meetings and conferences held on impartial health research issues, will be curtailed.

Mr. Early. For example, are they creating problems for Dr. Pinn and Dr. Ruffin?

Dr. Healy. The trips that promote and foster the missions of the Office of Research on Women's Health and the Office of Minority Programs within the biomedical community have been curtailed and the opportunities to present NIH's position on women's and minority health will be declined.

HIRING AND PROMOTION OF WOMEN

Mr. Hoyer. Please provide for the record a table showing the distribution of scientists by sex for each pay plan and grade within pay plan for FY 1991 broken down by institute.

Dr. Healy. The following table is a distribution of scientists by sex for pay plans and grade levels for FY 91 by ICD.

DISTRIBUTION OF SCIENTISTS BY SEX
FOR PAY PLANS AND GRADE LEVELS
FY 1991

ICD	SES		CC 07-08		GS/GM 13-15		CC 05-06		ST/C 04	
	M	W	M	W	M	W	M	W	M	W
OD	12	1	0	0	22	8	1	0	1	0
ORS	0	0	0	0	2	2	0	0	0	0
NIA	7	2	0	0	49	14	9	0	3	1
NIAID	14	1	1	0	88	60	31	1	16	6
NIAMS	4	0	0	0	17	5	5	0	0	3
NCI	16	4	1	0	262	116	76	4	48	17
NICHD	10	2	0	0	48	27	9	0	13	7
NIDCD	4	0	0	0	4	4	0	0	0	0
NIDR	3	1	0	0	38	16	15	1	1	0
NIDDK	21	1	1	0	83	27	19	0	12	1
NEI	6	0	0	0	26	14	0	0	2	0
NIEHS	9	1	0	0	94	15	4	0	1	0
NIGMS	2	4	0	0	18	14	0	0	1	0
NHLBI	14	7	0	0	90	47	25	1	20	2
NCHGR	0	1	0	0	3	5	0	0	0	0
NINDS	14	0	0	0	64	19	17	0	5	2
NCNR	0	1	0	0	1	1	0	0	0	0
NCRR	1	1	0	0	19	9	0	0	0	0
FIC	1	0	0	0	7	4	0	0	0	0
NLM	3	0	0	0	23	3	1	0	1	0
CC	1	0	0	0	29	16	15	0	0	0
DCRT	1	0	0	0	16	0	1	0	1	0
DRG	1	0	0	0	91	27	0	0	0	0
TOTAL	144	27	3	0	1,094	453	228	7	125	39

M= MEN
W= WOMEN
SES= SENIOR EXECUTIVE SERVICE
CC 07-08= COMMISSIONED CORPS LEVELS 07-08
ST/C04= SCIENTIFIC/COMMISSIONED CORPS 04

Mr. Hoyer. Please provide a table showing the distribution by sex of senior level scientists with management responsibilities (GM-13 and above) broken down by Institute.

Dr. Healy. The following table is a distribution of senior level scientists (GS/GM 13 and above) by sex for each ICD.

DISTRIBUTION OF SENIOR LEVEL SCIENTISTS
(GS/GM-13 AND ABOVE)
FY 1991

ICD	SES		CC 07-08		GS/GM 13-15		TOTAL	
	M	W	M	W	M	W	M	W
OD	12	1	0	0	22	8	34	9
ORS	0	0	0	0	2	2	2	2
NIA	7	2	0	0	49	14	56	16
NIAID	14	1	1	0	88	60	103	61
NIAMS	4	0	0	0	17	5	21	5
NCI	16	4	1	0	262	116	279	120
NICHD	10	2	0	0	48	27	58	29
NIDCD	4	0	0	0	4	4	8	4
NIDR	3	1	0	0	38	16	41	17
NIDDK	21	1	1	0	83	27	105	28
NEI	6	0	0	0	26	14	32	14
NIEHS	9	1	0	0	94	15	103	16
NIGMS	2	4	0	0	18	14	20	18
NHLBI	14	7	0	0	90	47	104	54
NCHGR	0	1	0	0	3	5	3	6
NINDS	14	0	0	0	64	19	78	19
NCNR	0	1	0	0	1	1	1	2
NCRR	1	1	0	0	19	9	20	10
FIC	1	0	0	0	7	4	8	4
NLM	3	0	0	0	23	3	26	3
CC	1	0	0	0	29	16	30	16
DCRT	1	0	0	0	16	0	17	0
DRG	1	0	0	0	91	27	92	27
TOTAL	144	27	3	0	1,094	453	1,241	480

M= MEN
W= WOMEN
SES= SENIOR EXECUTIVE SERVICE
CC= COMMISSIONED CORPS
GS/GM= GENERAL SCHEDULE/MERIT PAY

STAFF FELLOWS

Mr. Hoyer. Over the past 5 years (FY 87 - FY 91), there have been 4,202 individuals in the NIH Staff Fellows Program. What has been the distribution of staff fellows by sex in each of the ICD's during this period?

Dr. Healy. The following table is a distribution of NIH Staff Fellows by sex for each ICD for FY 89 - FY 91. The data requested for FY 87 and FY 88 is not available by ICD.

NIH STAFF FELLOWS PROFILE BY SEX
FY 89 - FY 91

ICD	FY 89		FY 90		FY 91	
	MEN	WOMEN	MEN	WOMEN	MEN	WOMEN
OD	0	0	0	0	1	0
ORS	0	0	0	0	0	0
NIA	22	12	19	8	19	11
NIAID	78	20	69	24	63	22
NIAMS	10	4	11	4	11	4
NCI	138	53	117	62	125	68
NICHD	30	15	29	16	32	24
NIDCD	2	0	2	1	5	2
NIDR	19	15	16	15	19	15
NIDDK	61	23	47	18	41	25
NEI	16	8	17	9	18	9
NIEHS	29	16	34	17	32	19
NIGMS	11	7	5	12	5	11
NHLBI	78	26	48	25	46	29
NCHGR	0	0	0	0	0	0
NINDS	62	32	57	31	60	26
NCNR	0	0	0	0	0	0
NCRR	0	0	0	0	11	1
FIC	0	0	0	0	0	0
NLM	5	0	7	0	6	0
CC	20	6	8	8	7	8
DCRT	3	0	3	0	2	0
DRG	0	0	0	0	0	0
TOTAL	584	237	489	250	503	274

Mr. Hoyer. Of those fellows who were converted to permanent positions during this period, what was the distribution by sex in each of the ICDs?

Dr. Healy. The following table is a distribution of conversions of NIH staff fellows by sex for each ICD for FY 89 - FY 91. The data requested for FY 87 and FY 88 is not available by ICD.

CONVERSIONS OF NIH STAFF FELLOWS BY SEX
FY 89 - FY 91

ICD	FY 89		FY 90		FY 91	
	MEN	WOMEN	MEN	WOMEN	MEN	WOMEN
OD	0	1	0	0	0	0
ORS	0	0	0	0	0	0
NIA	5	1	0	2	0	1
NIAID	0	0	1	1	3	3
NIAMS	0	0	1	0	1	0
NCI	6	2	6	5	2	1
NICHD	0	0	1	0	0	0
NIDCD	0	0	0	0	0	0
NIDR	1	1	4	1	0	1
NIDDK	0	0	1	0	1	1
NEI	0	0	1	0	0	0
NIEHS	0	0	1	2	0	0
NIGMS	0	1	0	0	0	0
NHLBI	1	1	2	1	0	1
NCHGR	0	0	0	0	0	0
NINDS	3	2	3	0	0	0
NCNR	0	0	0	0	0	0
NCRR	0	0	0	0	0	0
FIC	0	0	0	0	0	0
NLM	0	0	0	0	1	0
CC	0	0	1	1	0	0
DCRT	0	0	0	0	0	0
DRG	0	0	0	0	0	0
TOTAL	16	9	22	13	8	8

Mr. Hoyer. Please provide for the record a table showing the distribution of intramural tenured scientists by sex for senior level (SES, Commissioned Corps 05-08, GS/GM 13-15) and mid-entry level (GS, Commissioned Corps 01-04) as of December 1991?

Dr. Healy. The following table is a distribution of intramural tenured scientists by sex for pay plans and grade levels as of December 1991.

DISTRIBUTION OF M.D AND PH.D EMPLOYEES BY SEX AS OF JANUARY 25, 1992

Permanent Workforce

DEGREE	MEN	WOMEN	TOTAL
M.D	321 (71%)	132 (29%)	453
PH.D	797 (68.5%)	367 (31.5%)	1,164

Temporary Workforce

DEGREE	MEN	WOMEN	TOTAL
M.D	18 (52.9%)	16 (47.1%)	34
PH.D	25 (55.6%)	20 (44.4%)	45

Total Workforce

DEGREE	MEN	WOMEN	TOTAL
M.D	339 (69.6%)	148 (30.4%)	487
PH.D	822 (68%)	387 (32%)	1,209

SALARIES

Mr. Hoyer. Based on reviews of average salary data in the professional occupational series for NIH in FY 91, men earned an average of $13,872 more than women. Please provide a table showing the average salaries for male and female employees in this series for the years FY 87 - FY 91.

Dr. Healy. The following table is a profile of average grade and salary by sex for NIH employees in professional series occupations for FY 88 - FY 91. The data requested for FY 87 is not available.

PROFILE OF AVERAGE GRADE AND SALARY BY SEX
PROFESSIONAL SERIES OCCUPATIONS
FY 88 - FY 91

YEAR	AVERAGE GRADE		AVERAGE SALARY	
	MEN	WOMEN	MEN	WOMEN
FY 88	13	11	$50,204	$36,138
FY 89	13	11	$52,451	$38,896
FY 90	13	11	$54,383	$41,182
FY 91	13	11	$57,149	$43,277

Mr. Hoyer. What is the distribution of M.D. and Ph.D. employees by sex and degree for the period FY 87 - FY 91?

Dr. Healy. The following table is a distribution of M.D. and Ph.D. employees by sex as of January 1992. The data requested for FY 87 - FY 91 is not available.

DISTRIBUTION OF INTRAMURAL TENURED SCIENTISTS BY SEX FOR PAY PLANS AND GRADE LEVELS AS OF DECEMBER 1991

PAY PLANS	GRADES	MEN	WOMEN	TOTAL
SES		90 (94.7%)	5 (5.2%)	95
CC	7-8	1 (100%)	0	1
GS/GM	13-15	602 (76.2%)	188 (23.7%)	790
CC	5-6	200 (97.5%)	5 (2.4%)	95
CC	1-4	9 (90.%)	1 (10%)	10

SES= Senior Executive Service
CC= Commissioned Corps
GS= General Schedule
GM= Merit Pay

WOMEN'S HEALTH RESEARCH

Mr. Hoyer. What major studies relating to either women's health or minority health issues are underway at each of the ICD's?

Dr. Healy. Major studies related to minority health in each of the ICDs are discussed in the report, Strengthening Minority Health Research and Research Training Activities at the National Institutes of Health. The report contains a detailed discussion of minority health research and research training initiatives in each of the ICDs. Once this report has been approved by the Office of the Secretary, Department of Health and Human Services, it will be forwarded to the House Committee and Appropriations.

This information is contained within The Advisory Committee on Women's Health Issues (ACWHI) Report on Gender Related Studies at the NIH. We are making a draft copy available to Mr. Hoyer's office. This report will, however, form one part of an overall first-year report from the Office of Research on Women's Health. This report will be presented in four sections: 1) a report on the office and its activities, 2) the ACWHI Report, 3) the Proceedings from the Workshop, Opportunities for Research on Women's Health, and 4) a report on the status of the Tracking System on the Inclusion of Women and Minorities in Clinical Studies. In addition, an executive summary will be available which presents an comprehensive account of information contained in the 4-volume report. The ORWH believes that this 4-part report presents a more complete picture of first-year ORWH activities rather than a piece-meal release of information. The total package is expected to be released in June 1992.

The ACWHI report does not necessarily delineate where minority women are included in studies. We would also point out that many of the studies now underway within the institutes are notable for their attempts to, and often their success in, including minority women in the research.

Mr. Hoyer. How specifically has each ICD been working with the Office of Research on Women's Health to identify needed and important research in this area?

The Institutes, Centers, and Divisions (ICDs) of the NIH have been most cooperative in working with the ORWH to carry out this long-needed research agenda on women's health. First, each ICD has sent a representative to serve on The Advisory Committee on Women's Health Issues (ACWHI), an advisory committee to the Director, ORWH. This group is an important one, for in addition to serving as an advisory group to the Director, ORWH, it also serves as a representative within each ICD from the ORWH. Several subcommittees have been formed within this group:

- a Subcommittee on Data acquisition and Management -- this group gathers information and data on women's health from available data sources and from within the NIH ICDs;
- a Subcommittee on ORWH Speaker's Roster -- this group devises a list of qualified speakers and prepares materials for them to use in fulfilling the numerous speaking engagements requests that come into the ORWH;
- A Subcommittee on the Women's Health and Behavior Seminar Series -- this group is preparing a series of seminars on women's health issues for presentation at NIH.

Second, each ICD has been asked to respond to a request from the Director, ORWH on potential projects available for funding supplementation or co-funding. This request is currently with the ICDs to be returned on April 27, 1992. This plan requests applications from the ICDs for funding research on women's health in the following ways:

1. Administrative Supplement. The ORWH will offer approximately $1.5 million in supplemental funds of up to $50,000 (total costs) per project for FY 1992. These administrative supplements are offered to enable currently funded investigators to: a) enhance targeted research efforts on specific diseases, disorders, or conditions which are described in The ORWH Research Agenda on Women's Health and which affect women's health across the life span; b) enhance the recruitment of women, particularly minority women, within an ongoing study, and/or, c) demonstrate the feasibility of innovative techniques for recruiting or retaining women in research studies.

2. Co-funding. The ORWH will offer approximately $3.5 million in funds of up to $100,000 (total costs) per project for co-funding, with the Institutes and Centers, grants, contracts, or cooperative agreements of investigators with new proposals in FY 1992. These funds are offered to enable investigators to: a) meet the

research agenda on specific diseases, disorders, or conditions which are described in The ORWH Research Agenda on Women's Health and which affect women's health across the life span, b) address special projects on topics identified as having special Congressional interest: uterine leiomyomata, endometriosis, HIV and AIDS in women, pelvic inflammatory disease, and sexually transmitted diseases; and c) deliberately expand the study population to include special populations of underserved women (for example, minority women, women in low-income situations, women in inner cities and rural areas).

3. Special Projects. The ORWH will offer approximately $2 million in amounts to be determined by the ORWH and the particular Institute for projects that have been designated by both the ORWH and that particular Institute as a high priority area for research on women's health. Such projects, already specified in The ORWH Research Agenda on Women's Health, might include, but are not limited to special issues in women's reproductive health, arthritis, immunology, cardiovascular disease and HIV and AIDS in women.

The process of receiving and reviewing the applications for supplementation or co-funding will take place during the spring with awards expected to be announced no later than the end of June. The Office is currently in the process of identifying representatives of Institutes to serve as reviewers for determining the actual awards.

In addition, the Office has been working with different groups within the ICDs to consider special projects that might be developed this year and next concerning specific women's health needs. These meetings include, but are not limited to, the Advisory Committee on Women's Health Issues (advisory committee to ORWH), different Advisory Councils of the NIH institutes, staff of the NIH institutes, centers, and divisions, with scientists from the extramural community, and with advocacy groups. This is in process now in preparation for FY 93 funding activities.

UNCONVENTIONAL MEDICAL PRACTICES

Mr. Smith. In the FY 1992 Appropriations Bill, $2 million was added to the Office of the Director of NIH with the "request that NIH establish within the Office of the Director an office "dedicated to the investigation and validation of unconventional medical practices". What action has been taken to address this request?

Dr. Healy. NIH plans to establish an Office of Unconventional Medical Practices (UMPs) in the Office of Science Policy and Legislation. The steps to accomplish this are underway, and should be implemented by May. The Office of Unconventional Medical Practices will identify projected resources, including staffing and funding requirements, steps to be taken and their timing in securing external advice, and an agenda that will guide the evaluation of unconventional medical practices.

The language in the Fiscal Year 1992 NIH Appropriations Bill directs NIH to establish and convene an advisory committee to screen and select the procedures for investigation and to recommend a research program to fully test the most promising UMPs. NIH has been actively soliciting members to serve on this Committee. The first meeting of the Advisory Committee on Unconventional Medical Practices has been scheduled for June 17-18 at the NIH. This meeting will be open to the public. Subsequent meetings will have an open public forum as a major component to receive suggestions from the public, advocates, and opponents to UMPs.

Consistent with its role as a world leader in biomedical research, the NIH is prepared to offer technical assistance and financial resources for scientifically rigorous evaluation of claims made on behalf of UMPs.

Mr. Smith. Do you plan to establish a permanent office?

Dr. Healy. Yes, as I have indicated, the Office of Unconventional Medical Practices will be established by May.

Mr. Smith. If so, what will be its organizational makeup and its duties?

Dr. Healy. Several activities have been identified to fulfill the mandate provided by the Senate and the House of Representatives. NIH is prepared to encourage more research in UMPs and will do so through the activities that are presented briefly in the following discussion.

Support for Pilot Studies

The NIH is committed to assisting the advocates of unconventional medical practices to develop objective, scientific data that will permit fair evaluations of their merit. As is the case for more conventional therapies, these data can be generated by smaller pilot studies. If promising results ensue, the data from these small pilot studies could be used in support of grant applications to conduct larger controlled studies that are required to establish with certainty the safety and effectiveness of a treatment or diagnostic procedure.

Advisory Committee on Unconventional Medical Practices

In addition to the first scheduled meeting of the Committee in June, a three day planning workshop on specific UMPs will be conducted in September of 1992 to determine the current state of knowledge and to assist in the development of methods to investigate or evaluate the UMPs. One of the goals of this activity is to provide assistance to practitioners and advocates of UMPs in their efforts to develop objective, scientific data for the purpose of establishing the potential usefulness of specific alternative medical practices. Such support can take a variety of forms. Existing evaluation models or new evaluation methods may serve as a basis for the evaluation of UMPs. In some cases these assessments may include quality of life assessments, self-improvement rating scales, or other newly developed indices.

Inventory of Unconventional Medical Practices Research Supported by the National Institutes of Health

Prior to the first meeting of the Subcommittee on Unconventional Medical Practices, NIH will complete the survey of ICDs to determine the extent and level of support for UMPs. Results from this survey would provide baseline information on the resources currently being devoted to these types of therapies by the NIH. However, some would suggest that once a treatment is being objectively evaluated by the NIH it may no longer be considered "unconventional".

Determining the Extent of Utilization of Unconventional Medical Practices by the Public

Formal studies will be developed to determine the extent to which UMPS are used by the public. These will include both prospective studies and retrospective reviews of the literature and existing data bases to define the extent of utilization of these services in the United States.

Coordination of Unconventional Medical Practices Activities at the National Institutes of Health

In light of the many and diverse UMPS that may be under consideration at any one given time, no one Institute will assume the lead role in this activity. Individuals from each of the Institutes, Centers, and Divisions have been requested to assist with the coordination of these activities. Four staff members will be assigned the responsibility to implement these activities within the Office of Unconventional Medical Practices.

IMPACT OF CLINICAL CENTER REPLACEMENT

Mr. McDade. Dr. Healy, you have stated that the NIH Clinical Center requires complete replacement, as opposed to extensive renovation. Since a high priority at NIH is always research project grants, or RPG's, can you tell the Committee how many RPG's NIH would not be able to fund if the replacement option were selected?

Dr. Healy. The total amount of funds available for competing RPGs, $1.3 billion, is less than the replacement cost of the Clinical Center, $1.6 billion. If construction costs were phased in over time, however, the annual amount would likely not exceed the total amount for competing RPG's.

Mr. McDade. If the extensive renovation option were pursued? If these figures are not available today, please submit them for the record, including all relevant assumptions.

Dr. Healy. If the renovation option were pursued at a cost of $1.2 billion, approximately 5,200 out of 5,800 RPGs would not be funded. As above, if construction costs were phased in over time, fewer RPG's would have to be sacrificed.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Office of the Director

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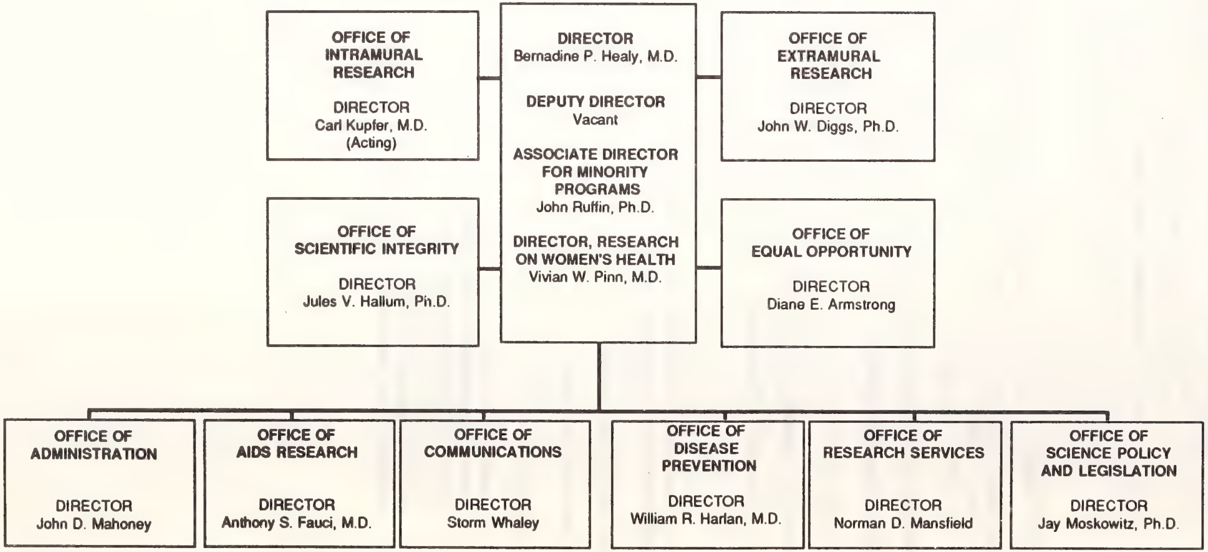
National Institutes of Health
Office of the Director
Organization Structure


OFFICE OF INTRAMURAL RESEARCH
DIRECTOR Carl Kupfer, M.D. (Acting)
DIRECTOR Bernadine P. Healy, M.D.
DEPUTY DIRECTOR Vacant
ASSOCIATE DIRECTOR FOR MINORITY PROGRAMS John Ruffin, Ph.D.
DIRECTOR, RESEARCH ON WOMEN'S HEALTH Vivian W. Pinn, M.D.
OFFICE OF EXTRAMURAL RESEARCH
DIRECTOR John W. Diggs, Ph.D.
OFFICE OF SCIENTIFIC INTEGRITY
DIRECTOR Jules V. Hallum, Ph.D.
OFFICE OF EQUAL OPPORTUNITY
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OFFICE OF AIDS RESEARCH
DIRECTOR Anthony S. Fauci, M.D.
OFFICE OF COMMUNICATIONS
DIRECTOR Storm Whaley
OFFICE OF DISEASE PREVENTION
DIRECTOR William R. Harlan, M.D.
OFFICE OF RESEARCH SERVICES
DIRECTOR Norman D. Mansfield
OFFICE OF SCIENCE POLICY AND LEGISLATION
DIRECTOR Jay Moskowitz, Ph.D.

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NATIONAL INSTITUTES OF HEALTH

Office of the Director

For carrying out the responsibilities of the Office of the Director, National Institutes of Health, [$143,313,000, of which $25,000,000 shall be for the support of the women's health study and shall remain available until September 30, 1993] $203,430,000: Provided, That of the funds made available under this heading, $12,500,000 shall not become available for obligation until September 30, [1992] *1993*: Provided further, That funding shall be available for the purchase of not to exceed five passenger motor vehicles for replacement only: [Provided further, That $7,500,000 of this amount shall be available for extramural facilities construction grants if awarded competitively:] Provided further, That the Director may direct up to 1 percent of the total amount made available in this Act to all National Institutes of Health appropriations to [emergency] *high priority* activities the Director may so designate: Provided further, That no such Appropriation shall be increased or decreased by more than 1 percent by any such transfers and that the Congress is promptly notified of the transfer.

(Departments of Labor, Health and Human Services and Education, and Related Agencies Appropriations Act, 1992.)

NATIONAL INSTITUTES OF HEALTH

Office of the Director

Amounts Available for Obligation 1/

	1991 Actual	1992 Appropriation	1993 Estimate
Appropriation....................	$100,575,000	$143,313,000	$203,430,000
Sequester order................	-1,000	---	---
Section 514(a) reduction.......	-500,000	---	---
Section 514(b) reduction.......	-2,424,000	---	---
Section 214 travel reduction...	---	-76,000	---
Section 513(a) travel reduction	---	-125,000	---
Section 513(a) S&E reduction...	---	-1,000,000	---
Subtotal, adjusted appropriation..............	97,650,000	142,112,000	203,430,000
Unobligated balance start of year........................	---	1,506,000	---
Unobligated balance end of year........................	-1,506,000	---	---
Unobligated balance lapsing......................	-291,000	---	---
Total obligations..........	95,853,000	143,618,000	203,430,000

1/ Excludes the following amounts for reimbursable activities carried out under this account: FY 1991 - $33,608,000; FY 1992 - $68,100,000; FY 1993 - $68,100,000. The FY 1991 actual, the FY 1992 appropriation and FY 1993 estimate excludes $513,000, $854,000 and $882,000, respectively in permanent budget authority expected to be realized from Cooperative Research and Development Agreements.

NATIONAL INSTITUTES OF HEALTH

Office of the Director

Budget Mechanism
(Dollars in thousands)

	1991 Actual		1992 Appropriation		1993 Estimate	
	FTE	Amount	FTE	Amount	FTE	Amount
Research Management and Support....................	638	$97,650	665	$142,112	685	$203,430
OD Operations....................	(638)	(50,511)	(646)	(55,240)	(655)	(57,224)
Director's Discretionary Fund....		(19,252)		(17,913)		(20,000)
Extramural Construction..........		(14,438)		(7,500)		---
Academic Research Enhancement Award Program..................		(13,449)		(14,256)		(14,256)
Science Education................		---	(2)	(1,980)	(4)	(1,980)
Minority Programs................		---	(6)	(10,236)	(8)	(10,236)
Research on Women's Health.......		---	(7)	(10,240)	(8)	(10,240)
Women's Health Study.............		---	(4)	(24,747)	(8)	(44,494)
Minority Health Initiative.......		---		---	(2)	(45,000)
Total Budget Authority......	638	97,650	665	142,112	685	203,430

NATIONAL INSTITUTES OF HEALTH

Office of the Director

CROSSWALK - 1991 Actual
(Dollars in thousands)

PROGRAM ACTIVITY	Mechanism Research Management and Support	Total
Research Management and Support	$97,650	$97,650
Total	97,650	97,650

NATIONAL INSTITUTES OF HEALTH

Office of the Director

CROSSWALK - 1992 Appropriation
(Dollars in thousands)

	Mechanism	
PROGRAM ACTIVITY	Research Management and Support	Total
Research Management and Support....................	$142,112	$142,112
Total....................................	142,112	142,112

NATIONAL INSTITUTES OF HEALTH

Office of the Director

CROSSWALK - 1993 Estimate
(Dollars in thousands)

	Mechanism	
PROGRAM ACTIVITY	Research Management and Support	Total
Research Management and Support	$203,430	$203,430
Total	203,430	203,430

NATIONAL INSTITUTES OF HEALTH

Office of the Director

Summary of Changes

1992 Estimated budget authority	$142,112,000
1993 Estimated budget authority	203,430,000
Net Change	+61,318,000

	1992 Current Estimate Base		Change from Base	
	Pos. (FTE)	Budget Authority	Pos. (FTE)	Budget Authority
Changes:				
A. Built-in:				
1. Annualization of FY 1992 pay raise		$35,584,000		+$363,000
2. Within grade increase		35,584,000		+ 382,000
3. FY 1993 pay raise		35,584,000		+ 979,000
4. One extra day of pay		35,584,000		- 132,000
5. Increased cost of services and supplies		96,852,000		+3,857,000
6. Service and Supply Fund increase		2,176,000		+170,000
Subtotal				+5,619,000
	No.	Amount	No.	Amount
B. Program:				
1. Women's Health Study	(4)	24,747,000	(+4)	+19,423,000
2. Minority Health Initiative	--	--	(+2)	+45,000,000
3. Office of Human Subjects Research	--	--	(+4)	+395,000
4. Office of Scientific Integrity	16	1,655,000	(+5)	+255,000
5. Ethics Office	--	--		+106,000
6. Office of Research on Women's Health	(7)	10,240,000	(+1)	--
7. Minority Programs	(6)	10,236,000	(+2)	--
8. Science Education	(2)	1,980,000	(+2)	--
9. Extramural Facilities Construction Grants	--	7,500,000		-7,500,000
10. OD Operations -- Unconventional Medical Practices	--	1,980,000		-1,980,000
Subtotal			(+20)	+55,699,000
Total Changes			(+20)	+61,318,000

NATIONAL INSTITUTES OF HEALTH

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Budget Authority by Activity
(Dollars in thousands)

	1991 1/ Actual		1992 1/ Appropriation		1993 1/ Estimate	
	FTE	Amount	FTE	Amount	FTE	Amount
Research Management and Support..............	638	$95,853	665	$143,618	685	$203,430
Unobligated balance start of year..................	---	---	---	-1,506	---	---
Unobligated balance end of year..................	---	1,506	---	---	---	---
Unobligated balance lapsing..................	---	291	---	---	---	---
Total budget authority...	638	97,650	665	142,112	685	203,430
HIV/AIDS...................	(30)	(13,243)	(42)	(13,701)	(42)	(14,372)

1/ The FY 1991 actual, the FY 1992 appropriation, and the FY 1993 estimate excludes $513,000 $854,000 and $882,000 respectively, in permanent budget authority expected to be realized from Cooperative Research and Development Agreements.

NATIONAL INSTITUTES OF HEALTH

Office of the Director

Budget Authority by Object

	1992 Appropriation	1993 Estimate	Increase or Decrease
Total number of full-time permanent positions..................	641	661	+20
Total compensable workyears: Full-time equivalent employment........	678	698	+20
Full-time equivalent of overtime and holiday hours...................	6	6	---
Average ES salary......................	$104,530	$109,677	+$5,147
Average GS/GM grade...................	12	12	---
Average salary, grades established by act of July 1, 1944 (42 USC 207)..	53,061	55,184	+2,123
Average salary of ungraded positions...	67,511	70,347	+2,836
Personnel Compensation:			
Full-time permanent.................	$26,113,000	$29,681,000	+$3,568,000
Other than full-time permanent.......	1,803,000	1,942,000	+139,000
Other personnel compensation.........	820,000	850,000	+30,000
Special personnel service payments...	142,000	150,000	+8,000
Total, personnel compensation......	28,878,000	32,623,000	+3,745,000
Personnel benefits....................	5,706,000	6,198,000	+492,000
Benefits for former personnel..........	37,000	39,000	+2,000
Travel and transportation of persons...	275,000	503,000	+228,000
Transportation of things..............	67,000	70,000	+3,000
Rent, communications and utilities.....	1,121,000	1,177,000	+56,000

Printing and reproduction...............	487,000	511,000	+24,000
Other services........................	102,694,000	159,290,000	+56,596,000
Supplies and materials................	640,000	672,000	+32,000
Equipment.............................	2,207,000	2,347,000	+140,000
Total budget authority by object.....	142,112,000	203,430,000	+61,318,000

NATIONAL INSTITUTES OF HEALTH

Office of the Director

Significant Items in the House, Senate and Conference Appropriations Committee Reports

Minority Health Emphasis and Reporting

The House in its report 102-121, pages 58-59 stated "...funds have been added for the newly established Office of Minority Health Research which can be allocated to initiate new research or to expand existing projects throughout the NIH. The minority health initiative, however, should not be viewed as being limited to efforts in this one Office. The Committee expects the Secretary and the new Director to make this an area of concern for every Institute and Center. In order to monitor both the degree of effort and progress against these goals, the Committee directs the Secretary to require each Institute to report annually to Congress through a consolidated report, approved by the Secretary, on activities in the area of minority health. The Committee believes that the report currently produced by the National Institute of Allergy and Infectious Diseases could be a model for such a report."

Action Taken or to be Taken: A report on these issues has been prepared and is in the process of being reviewed.

Pediatric Clinical Trials

The House in its report 102-121, page 81 stated "...The Committee, however, is very concerned that the level of cooperation and coordination among the various Institutes... The Committee expects a detailed report by January 1, 1992 on the division of labor among the Institutes regarding pediatric AIDS basic research, clinical trials, drug development, opportunistic infection, and other areas of interest and inquiry relating to pediatric AIDS. For example, the report is to include the level of resources devoted to these activities in each Institute. The Committee is very concerned that an overall research plan involving the relevant Institutes, especially NICHD, NIAID, and NCI, be developed in order to appropriately allocate future funds and against which to measure progress in this field."

Action Taken or to be Taken: A report on these issues is being prepared by NIH and will be submitted to the Committee.

Women's Health Study

The House in its report 102-121, page 102/103 stated "...The OD will coordinate a major new clinical trial in women's health...The leading causes of death and disability among America's women are cancer, cardiovascular disease, and osteoporosis. Although distinctly different problems, these disease are linked through specific potential preventive measures. The women's health study will address each of these areas, the impact preventive measures may have on these diseases, and the effects of such preventive measures in combination. The study will look at the effects on disease risk of changes in diet and exercise patterns, the use of hormones, and smoking cessation. The study will have three components, including a large surveillance program, a nationally based community prevention and intervention study, and randomized clinical trials. The Committee would like a report prior to the 1993 appropriation hearing providing more details on the design, implementation schedule, and cost estimates for the women's study."

Action Taken or to be Taken: A report addressing these issues has been prepared by NIH and has been submitted to the Committee.

Office of Research on Women's Health

The House in its report 102-121, page 103 stated "...The Committee has provided additional funding to the Office of Research on Women's Health to enhance research in several areas. The Committee intends that the Office determine the allocation of the funds among the Institutes and Centers of the NIH, giving priority to the following research areas: uterine fibroids, endometriosis, pelvic inflammatory disease (PID), the relationship between breast cancer and oral contraceptive use, women and AIDS and health effects on those exposed to the synthetic estrogen drug, DES.

Action Taken or to be Taken: The Office of Research on Women's Health (ORWH) is in the process of finalizing a year-long process of designing and implementing a trans-NIH research agenda on women's health, in cooperation with the Institute and Centers. The culmination of this process, which will be completed shortly, is the allocation of funds across the spectrum of women's health among the NIH Institutes and Centers. The funds will be distributed based upon the remarkably congruent recommendations from the scientific community, from priority research areas specified by Congress, and from organizations involved in women's health.

Diagnostic Radiology

The House in its report 102-121, page 104 stated "...The field of diagnostic radiology has played a significant role in the medical advances made over the past several decades. Medical imaging procedures, in fact, now contribute to the final patient diagnosis in more than 75 percent of all hospital admissions. Given the potential this field holds to more accurately and safely diagnose disease through non-invasive procedures, the Committee has called for the establishment of an intramural diagnostic radiology laboratory at NIH. The Committee is pleased to learn that such a laboratory will be fully operational with the next few months. The Committee now looks forward to receiving from NIH its recommendations on how to build upon the strengths of the intramural diagnostic radiology program and those of academic research centers. Such a private/public sector partnership will provide for optimum research findings in the field."

Action Taken or to be Taken: A report addressing these issues has been prepared by NIH and has been submitted to the Committee.

Sleep Disorders Research

The House in its report 102-121, page 105 stated "...The Committee has closely monitored the National Commission on Sleep Disorders Research in its attempt to develop a long-range plan. The Committee looks forward to reviewing the Commission's final report and considering its recommendations."

Actions Taken or to be Taken: The National Commission on Sleep Disorders Research will soon complete a developed long range plan. It is expected that the final plan will be forwarded to Congress in late spring or early summer of FY 1992 following the completion of the report document.

Financial Management Plan

The House in its report 102-121, page 57 stated "...The Committee has been told repeatedly by researchers that instead of managing costs by specific budget decisions, many Institutes have imposed artificial caps on the size of awards and routinely use across-the-board percentage cuts. The Committee is reassured by the new Director's attention to this issue and is hopeful that this is a transitional problem which will by fully corrected in 1992. If downward negotiation is to be eliminated, however, NIH will have to play a more aggressive role in analyzing the reasons for cost increases, in setting guidelines and policies about appropriate funding levels for certain types of expenditures, and in reviewing the budgets submitted by potential grantees. This is undoubtedly the most difficult task for the NIH in implementing the Financial Management Plan. It is also one of the most important. The Committee looks forward to hearing from the new Director on progress in this area when she appears to testify on her 1993 budget request. The Committee believes that this discussion should involve both the mechanisms for achieving cost control and the more fundamental question of whether the current average level of support per project is reasonable. This issue was initially raised by the Director at the 1992 hearings and it deserves more attention as Congress and the NIH discuss these issues."

Actions Taken or to be Taken: NIH has taken steps to eliminate uniform, across-the-board budgetary reductions. However, the elimination of uniform, across-the-board reductions is not synonymous with elimination of all budgetary adjustments following initial scientific review. Once initial review groups have made their reductions and staff has conducted its cost/price analysis and budgetary adjustments have been made to eliminate inaccurate, unallowable and inappropriate costs, there may still be a need for further reductions to meet the target number of grants intended by Congress.

While some grant programs do have caps on awards, such caps are established in advance, i.e., they are part of the program guidelines that are provided to investigators prior to the submission of applications. For example, a certain type of grant may not exceed a total of $350,000. The only other type of constraint that may be interpreted as a "cap" is the amount of increase that an ICD may provide in a competing continuation grant over the preceding non-competing grant. In balancing the need to provide adequate resources with the recognition that such resources are finite, an ICD may, when making a competing continuation award, take into consideration the level of support in prior years in determining the extent to which it can permit growth within current fiscal constraints. Such limits on growth will vary from program to program, depending on the opportunities and the resources available.

Indirect Costs

The House in its report 102-121, pages 57/58 stated "...The Committee has been greatly disturbed, as has the general public, with recent publicity regarding abuses by certain institutions in claiming reimbursement for costs under the indirect cost recovery system. As offensive as these specific cases are, however, the Committee is concerned that these may be merely the superficial signs of a systemic problem in which Federal grantees may have routinely cost-shifted non-research related expenses by claiming them under their indirect cost rates. Last year, this Committee identified indirect costs as an area of concern and the new Director testifying in April of this year identified indirect costs as her first priority in improving financial management at the NIH. She promised action within 45 days. The Committee was pleased to see the NIH, in cooperation with the Department and the OMB, meet this goal and move aggressively to modify federal indirect cost regulations... The Committee believes this is an effective first step but also agrees with the Director that a more thorough, long term review must be undertaken. This next step must deal directly with the broad area of facilities renovation and replacement in a thoughtful way. The Committee looks forward to further action on this problem over the next year. A failure to act could threaten public support for biomedical research in this country."

Actions Taken or to be Taken: The Department of Health and Human Services (DHHS) Working Group on the Costs of Research was formed by the DHHS in April 1991. Its task is to develop a comprehensive set of recommendations on future policies governing the reimbursement of indirect costs within the context of the total costs of supporting research. The group is comprised of the Assistant Secretary of Management and Budget, the Inspector General, and the Director of NIH.

The DHHS Working Group has initiated a plan to be conducted in three phases: (1) characterizing the current system of indirect costs reimbursement; (2) evaluating alternative reimbursement models; and (3) developing a report to the Secretary with recommendations on appropriate actions. In developing the report, various consultations with industry, academia and the non-profit sector were held. It is the intention that this report will provide valuable information to the Office of Management and Budget as they define future government-wide policies on indirect cost reimbursement.

Award Rates and Success Rates

The House in its report 102-121, page 58 stated "...Last year the House requested that NIH consider changes in the peer review system to ensure that study sections "approve" only those proposals which they considered deserving of public support both on technical grounds and based on their "inherent value" to biomedical research. This followed testimony by NIH that 95 percent of applications were being approved even though only 45-50 percent were considered scientifically "strong." NIH, in response to this request proposed to shift to a success rate method of counting grants. This "success rate" indicates the proportion of all grants submitted, good or poor, which were, or could be, funded. Success rates, while useful, do not tell either the Congress or the NIH what portion of the applications which are deserving of support can actually be funded. The Committee believes that the new Director should review this policy as she sets spending policies for 1992. Peer review is regarded as the cornerstone of the system for distributing Federal biomedical research resources. It does not seem unreasonable to ask a peer review panel to advise the NIH whether a project is technically sound, important to biomedical science, fiscally reasonable and deserving of support with public funds."

Actions Taken or to be Taken: In accordance with the NIH Financial Management Plan published in June 1991, NIH has begun to use success rates to represent the ratio of applications funded to applications reviewed. This is consistent with the practice of other federal funding agencies which have traditionally used success rates to show the proportion of total grant applications that result in funding. As part of its decision to adopt usage of the success rate, NIH also introduced some other changes in its initial review process. The concept of "approving" and "disapproving" grant applications has been abolished and, in its place, initial review groups are now able to "not recommend for further consideration" (NRFC) any application that does not have significant and substantial scientific merit and those applications that present biohazards, serious ethical problems, etc. Applications with NRFC designations are not reviewed by Councils or Boards and consequently, unfundable. All other applications receive a priority score and a percentile ranking.

In response to the Committee's interest in "portion of the applications which are deserving of support can actually be funded", NIH could provide data on the number of applications reviewed in any fiscal year that receive priority scores/percentile rankings, i.e., applications that could be considered "deserving of support". From that number, NIH could compute the percentage that actually resulted in funding. However, as a practical matter, Councils and Boards no longer routinely review the bottom one-third of those applications that are scored, i.e., those applications with a percentile ranking of 65 or beyond. Although any given application within the bottom tier can be singled out for funding consideration, the overwhelming majority of these grant proposals are never funded.

Acquired Immune Deficiency Syndrome-Women and HIV

The House in its report 102-121, page 59 stated "...the Committee encourages the NIH to develop a research initiative that would support research concerning the transmission, development, treatment, and prevention of HIV infection and related conditions in women. Little research has been devoted to HIV/AIDS in women, despite anecdotal reports that HIV manifests itself differently in women and that outcomes in women may differ from their male counterparts. Almost no research has been done on new chemical and physical barriers to HIV infection that might address these concerns for women."

Actions Taken or to be Taken: The NIH is increasing its study of HIV in women, a major objective of which is to determine how HIV disease may differ in women compared to men. Ongoing efforts include a priority on the inclusion of women and minorities in NIH-sponsored clinical trials, which is a requirement associated with the recompetition of the NIAID-sponsored adult units of the AIDS Clinical Trials Group (ACTG). Additionally, a number of NIH components, including the NIAID, the NICHD, and the NCI, have joined with other Public Health Service components, especially the Centers for Disease Control, to form a PHS Women and AIDS Study Group. The group is organizing a core collection of data on women and HIV infection. The NIAID and the CDC are planning a multi-site interagency women's cohort study to include 2,500 HIV-positive women and a comparison group of 500 HIV-negative women. This study is designed to describe the full spectrum of HIV infection in women, examine the potential co-factors affecting decline of immune function in women, and identify variables associated with survival. Phase I of this study is ongoing and involves the review of existing data from several NIAID-sponsored epidemiological studies of women. The specific objectives of the new initiative are: to identify the nature and rate of HIV disease progression in women; to determine the frequency, severity, and duration of women-specific conditions that are likely to be associated with or exacerbated by HIV infection (i.e., cervical disease, fungal infections of the genital tract, pelvic inflammatory disease, and sexually transmitted diseases; and to assess the effect of anti-retroviral or other drug therapy on the health and survival of women with HIV, and on the level of surrogate markers of disease progression.

Brain Tumor Research

The House in its report 102-121, pages 104/105 stated "...The Committee has heard testimony regarding the need for improved techniques for treating brain tumors. These tumors affect all ages but can be particularly damaging in young adults. The Committee believes that the development of improved methods for treating these tumors could save many lives, improve the quality of life for these patients, and lower health care costs. The Committee encourages the National Institute of Neurological Disorders and Stroke and the National Cancer Institute to accelerate their work in this area."

Actions Taken or to be Taken: The NCI currently supports an active clinical trial program for the treatment of brain and central nervous system (CNS) tumors through the Brain Tumor Cooperative Group. Brain tumor studies to be done in collaboration with the National Institute of Neurological Disorders and Stroke (NINDS) are in the early planning stages and the NCI and NINDS are also involved in cooperative efforts to develop an NIH-wide 5-year research plan for brain tumor imaging. Ongoing research includes evaluation of new chemotherapy drugs for CNS tumor activity, and the evaluation of differentiating agents such as retinoids in brain tumors. Also under development are radiation sensitizers to improve the efficacy of radiation therapy for brain tumors and radioprotectors for which there is some evidence that they may protect normal brain tissue but not tumor tissue.

The NINDS issued a request for applications (RFA) for feasibility grants for brain tumor research centers in September 1991. Applications are due January 1992. This effort will expedite the formation of clinical research centers that can develop new interdisciplinary research capabilities and methods relevant to the study of brain tumors. The centers will be a focus for research on improved diagnosis and management of patients. This effort is in addition to ongoing brain tumor research supported and conducted by the NINDS.

Chronic Fatigue Syndrome

The House in its report 102-121, page 105 stated "...The Committee is concerned that no study section exists to evaluate Chronic Fatigue Syndrome research proposals. The Committee requests the Office of the Director to evaluate the merits of establishing a multidisciplinary study section for Chronic Fatigue Syndrome."

Actions Taken or to be Taken: The Office of the Director convened a group of officials from the Office of Extramural Research, National Institute of Allergy and Infectious Diseases, and Division of Research Grants, to review needs for a multidisciplinary study section to evaluate Chronic Fatigue Syndrome research proposals. It was concluded that such a new study section should not be established at this time, especially in view of the small

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numbers and wide diversity of applications received each year. Participation of NIH officials in the DHHS and NIH Chronic Fatigue Syndrome Coordinating Committees will continue.

Demographic Research at NIH

The House in its report 102-121, page 105 stated "...The United States faces critical health care problems that have demographic, social and behavioral dimensions which merit systematic study. The Committee reiterates its support for demographic research at NIH, particularly at NICHD and NIA, as core elements of NIH's institutional mandate."

Actions Taken or to be Taken: The demographic studies supported by the NIA develop information that is essential to develop an understanding of the older population, as well as sub-populations such as older minorities and the "oldest-old", which is that group over the age of 85. Knowledge gained from these studies is invaluable for the rational development of many of the other research studies supported by the NIA.

The demographic studies supported by NICHD produce comprehensive information regarding the health and well-being of the population and provide a policy-relevant perspective for much of the biomedical research supported by the other programs in the Institute. In recent years, demographic studies have addressed such problems as: child care, infant mortality, reproductive health, AIDS and other sexually transmitted diseases, teenaged pregnancy, the effect of family disruption on child well-being, the interrelationship of nutritional status to fertility and child health, contraception, the health and well-being of minority groups, the interrelationship of immigration to health status and assimilation, and the relationship of intergenerational family processes to child development and success in the lifecourse.

Coordination of Pediatric AIDS Resources

The Senate in its report 102-104, page 111 stated "...The Committee, however, is very concerned that the level of cooperation and coordination among the various Institutes improve in order to assure the Committee that the expanded resources provided to the institutes in the area of pediatric AIDS are being appropriately distributed and most productively expanded. The Committee expects a detailed report by January 1, 1992 on the division of labor among the Institutes regarding pediatric AIDS basic research, clinical trials, drug development, opportunistic infection and other areas of interest and inquiry relating to pediatric AIDS. For example, the report is to include the level of resources devoted to these activities in each Institute."

Action Taken or to be Taken: A report on these issues is being prepared by NIH and will be submitted to the Committee.

Women's Health Study

The Senate in its report 102-104, page 145 stated "...Additionally, the Committee is concerned, however, that the women's health trial not supplant other important studies and research on women that needs to be done. The General Accounting Office reported to Congress that the lack of attention to women's health issues rested not simply with the fact that specific research on women was not being accomplished, but that too little attention was being focused on studying gender difference across the board the Committee requests a report from the Director of NIH as to the timing and implementation of this large-scale, multi-center trial."

Action Taken or to be Taken: A report addressing these issues has been prepared by NIH and has been submitted to the Committee.

5-Year Plan for HIV-Related Research Needs

The Senate in its report 102-104, page 149 stated "...The Committee commends the recent efforts by the National Academy of Sciences/Institute of Medicine to study the NIH AIDS program and recommend improvements. A major recommendation of this study was that the NIH develop a 5-year plan to identify HIV-related research needs and opportunities, set priorities, assess program balance, identify gaps in the NIH program, allocate resources and evaluate progress. The Committee requests the Director of NIH to undertake such an effort immediately, and submit a plan to the Committee within the year."

Action Taken or to be Taken: An initial plan has been developed and is currently being reviewed by the AIDS Program Advisory Committee. The committee will examine the draft plan and will identify priorities. It is anticipated that a completed plan will be provided by June 1992.

Health and Behavior

The Senate in its report 102-104, page 149 stated "...In 1990, the Congress received an interim report from the NIH working group on health and behavior, reporting that according to its recent calculations, approximately 4.3 percent of the NIH budget was spent on health and behavior research to the various Institutes in fiscal year 1989. The Committee has learned that the percentage dedicated to this important research is actually going down. The administration's fiscal year 1992 budget request for health and behavior research is less that 4.1 percent of the budget. The NIH is directed to redouble the efforts to increase the percentage of funds it spends on health and behavior research within the next 3 years, and to report to this Committee by March 30, 1992, on the ways in which it will reach that target, classifying research using the same principles employed in the 1990 report."

Action Taken or to be Taken: A draft report has been prepared in response to the Senate Appropriations Committee request. The report is being reviewed by the NIH Office of Disease Prevention and it is anticipated that the report will be completed by March 1992.

Representation of Advisory Boards and Commissions

The Senate in its report 102-104, page 149 stated "...The Committee is concerned that the membership of advisory boards and commissions within the Department of Health and Human Services and among other related Federal agencies, does not include broad representation of certain health care providers, including chiropractors. The Committee, therefore, directs the Department and other related agencies covered by this Appropriations Act to include a significantly larger number of chiropractors and other health care providers on all current and future advisory boards, commissions, and peer review panels. The Committee expects to receive periodic reports during the course of fiscal year 1992 regarding the implementation of this directive."

Action Taken or to be Taken: A report on these issues is being prepared by NIH and will be submitted to the Committee.

Diagnostic Radiology

The Senate in its report 102-104, page 150 stated "...the Committee has called for the establishment of an intramural diagnostic radiology laboratory at NIH. The Committee is pleased to learn that such a laboratory will be fully operational within the next few months. With the establishment of the intramural program, the Committee now expects NIH to move forward with an extramural grant program in this field in order to build upon the strengths of diagnostic radiology departments in academic research centers. The Committee expects that the appropriations committee will receive a report on the status of the intramural program prior to next year's hearings."

Action Taken or to be Taken: A report addressing these issues has been prepared by NIH and has been submitted to the Committee.

Discretionary Fund

The House and Senate Conference Appropriations Committee in report 102-282, on page 29 stated "...The conferees encourage the Director to use a portion of the discretionary fund for the James A. Shannon Director's Award Program.

Action Taken or to be Taken: The FY 1991 James A. Shannon Director's Award Program was highly successful and well received by the extramural scientific community. The Director will continue the program in FY 1992 and intends to use a considerable portion of the Director's Discretionary Fund for this purpose.

DES-Exposed Populations

The House and Senate Conference Appropriations Committee in report 102-282, on page 29 stated "...The conferees are agreed that research on DES-exposed populations be a priority for the NIH. The conferees recommend coordination between the NCI, NIEHS, and NICHD in the implementation of longitudinal studies to determine the risk of cancers in DES-exposed offspring and mothers, evidence of late recurrences of clear cell cancer, and the effects of DES on the immune and endocrine systems.

Action Taken or to be Taken: The National Cancer Institute, along with the National Institute of Child Health and Human Development and the National Institute of Environmental Health Sciences will sponsor a workshop in April 1992 to review current knowledge on DES-associated health outcomes in exposed mothers and in their children, and to establish recommendations for future research. Planning for this workshop, which will involve both intramural and extramural research communities, is currently underway.

Coordination Between Agencies

The House and Senate Conference Appropriations Committees in report 102-282, on page 29 stated "...The conferees agree that the Office of Research on Women's Health should coordinate with the NIH Office of Research on Minority Health and the Office of Minority Health in the Office of the Assistant Secretary for Health to ensure that resources are targeted appropriately and effectively.

Action Taken or to be Taken: The Office of Research on Women's Health and the Office of Minority Programs coordinate efforts to assure that resources for each office are allocated effectively and cooperative efforts are thereby maximized. In addition, information on these initiatives and activities is made available from both offices to the Office of Minority Programs (OASH) and the Office on Women's Health (OASH), in an effort to optimize efforts directed toward women and minorities. Such activities include, but are not limited to the following:

- establishment of the Committee on the Inclusion of Women and Minorities in Research, co-chairs by the Office of Research on Women's Health and the Office of Minority Programs along with the Office of Extramural Research;

- joint monitoring of the NIH Tracking System on the Inclusion of Women and Minorities in Research;

- consideration of co-funding on NIH research initiatives which address health issues among minority women.

Sharing Agreements

The House and Senate Conference Appropriations Committees in report 102-282, on pages 29/30 stated "...The conferees are aware of numerous, highly successful sharing agreements between the NIH clinical center and the Bethesda Naval Hospital, and understand that the NIH clinical center operates a fully integrated hospital information system. The conferees encourage the Director to continue and to expand these types of agreements, particularly in the area of medical automation and patient care.

Action Taken or to be Taken: The Clinical Center will continue to explore avenues of cooperation with the Bethesda Naval Hospital, taking advantage of it's unique geographical location particularly in matters of patient care. The medical information system of the Clinical Center (CCMIS) has been used for the past 15 years to support patient care and clinical research. The system is continually upgraded to provide timely automated medical information to the NIH user community. In preparation for Operation Desert Storm, the Clinical Center trained surgeons from the Bethesda Naval Hospital to use the CCMIS should that have become necessary. We will certainly participate in any areas of mutual benefit of the two hospitals in the applications of advanced computer technology to medical care.

Cost Control

The House and Senate Conference Appropriations Committees in report 102-282, page 30 stated "...The conferees reiterate the guidance provided last year regarding cost control and financial management and specifically urge the elimination of downward negotiations. The Institutes, through their study sections and advisory councils, should aggressively eliminate any costs which they believe are unnecessary. Once this is done, a grant or center should be funded at the full level without arbitrary reductions.

Action Taken or to be Taken: For FY 1992, NIH has developed a set of core principles to guide Institutes and Centers in making their research project grant awards. These principles state that, in awarding competing grants, Institutes/Centers will make those budgetary reductions that are a result of initial review and Council review recommendations, staff determinations of cost allowability and reasonableness and, where necessary, programmatic adjustments. There will no longer be uniform, flat-rate, across-the-board reductions, formerly referred to as "downward negotiations".

NATIONAL INSTITUTES OF HEALTH

Office of the Director

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1992 Amount Authorized	1992 Appropriation	1993 Amount Authorized	1993 Budget Estimate
Funded Authorizations:						
Office of the Director..............	Title IV, Section 402(b)	40 USC282	Indefinite	$142,112,000	Indefinite	$203,430,000
Total Budget Authority...				$142,112,000		$203,430,000

NATIONAL INSTITUTES OF HEALTH

Office of the Director

Appropriations History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1983	$24,283,000	$24,683,000	$24,683,000	$24,683,000
1984	26,720,000	26,779,000	26,720,000	26,720,000
1985	27,509,000	47,509,000	38,304,000	37,082,000 2/
1986	37,085,000	117,085,000	37,574,000	133,189,000 3/
1986 Sequester				-5,031,000
1987	36,701,000	246,651,000	56,708,000	57,463,000 4/5/
1988	59,819,000	71,389,000 6/	61,284,000	61,819,000
1989	59,578,000	71,578,000	65,578,000	72,201,000
1990	96,570,000	106,987,000	127,570,000	108,468,000 7/
1990 Sequester				-1,049,000
1991	82,975,000	106,175,000	77,975,000	97,651,000 8/9/
1991 Sequester				-1,000
1992	95,176,000	149,176,000	125,724,000	142,112,000 10/
1993	203,430,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.

2/ Includes $10,000,000 for the initiation of a program that supports biomedical research in small and minority schools and universities.

3/ Includes $20,000,000 for the continuation of a program that supports biomedical research in small and minority schools and universities, and $70,000,000 for research on AIDS. Includes $16,197,000 transfer from HRSA for establishment of the National Center for Nursing Research.

4/ Includes a transfer of $755,000 to cover the FERS increase and partial costs of the pay raise.

5/ The Budget Estimate to Congress proposed that all funding for AIDS research be consolidated in the Office of the Assistant Secretary for Health. The House Allowance consolidated all NIH AIDS funding in the Office of the Director, NIH; the Senate Allowance and the Appropriation spread the funding among the Institutes.

6/ Does not include funding for AIDS research. Consolidated at the Secretary's level.

7/ Excludes enacted administrative reduction of $519,000.

8/ Excludes enacted administrative reductions of $2,924,000.

9/ The FY 1991 and FY 1992 appropriations and FY 1993 estimates excludes $513,000, $854,000 and $882,000, respectively, in permanent budget authority expected to be realized from Cooperative Research and Development Agreements.

10/ Excludes enacted administrative reductions of $1,201,000.

Justification

Office of the Director

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
638	$97,650,000	665	$142,112,000	685	$203,430,000	+20	+$61,318,000

General Statement

The appropriation for the Office of the Director (OD) of the National Institutes of Health (NIH) provides funds for the central administration of, and services to, the NIH Institutes, Centers and Divisions (ICDs). While each major research component of the NIH administers the activities associated with its specific programs, the Office of the Director is responsible for their overall direction and coordination. The major units within the OD are responsible for central functions such as extramural and intramural research policy and the coordination of scientific inquiry; coordination of NIH AIDS research and establishment of associated policies and procedures; coordination and direction of research on women's health issues and minority research and training programs; analysis of legislation, program planning and evaluation; coordination of public affairs and communication activities; contract and grant administration; and financial and personnel management; and a number of other offices are responsible for promotion of disease prevention, nutrition research and medical applications of research and for NIH-wide direction and centralized services in such areas as equal opportunity and the promulgation of policies and procedures related to prevention and investigation of misconduct in science.

Funding for the Office of the Director during the last five years has been as follows:

	Amount	FTE
FY 1988	$61,819,000	514
FY 1989	72,201,000	558
FY 1990	89,916,000	598
FY 1991	97,650,000	638
FY 1992	142,112,000	665

270

Purpose and Method of Operation

The Office of the Director (OD) provides leadership, focus and direction to the NIH research community, and coordinates and directs initiatives which cut across the Institutes, Centers and Divisions of NIH. The OD is responsible for the development and management of intramural and extramural research and research training policy, the review of program quality and effectiveness, the coordination of selected NIH-wide program activities, and the administration of centralized support activities essential to operations of the NIH.

Several offices in the OD provide policy and direction to the NIH research community:

The Office of Extramural Research (OER) provides guidance in the development and management of extramural (grant, cooperative agreement and contract) research and training programs. The Office for Protection from Research Risks, (OPRR) in the OER, has the responsibility to develop and implement regulations and policies for the protection of human subjects and laboratory animals in all institutions that carry out research with resources from the Department of Health and Human Services.

The Office of Intramural Research implements and coordinates intramural research policy and programs, develops and coordinates intramural training and recruitment, provides staff support to the NIH Scientific Directors, represents the intramural programs on task groups and ad hoc committees and provides overall direction to the intramural research program. The Office of Human Subjects Research is being established within the Office of Intramural Research, as NIH's internal control, to coordinate and oversee the entire NIH human subjects protections system in order to ensure that research involving human subjects is carried out uniformly at NIH in accordance with the Code of Federal Regulations Title 45 Part 46 Protection of Human Subjects.

Through the Office of Disease Prevention (ODP), the OD coordinates activities concerning research related to disease prevention and promotion of disease prevention research; all aspects of nutrition research relating to the mission of NIH; and medical applications of research including drugs, procedures, devices, and other technology developed from basic biomedical research at NIH. The ODP has the responsibility for conducting the activities of Women's Health Study, a major, multi-year trans-NIH initiative that will address the prevention of cancer, heart disease, and osteoporosis in women.

The Office for Research on Women's Health (ORWH) develops NIH policy to ensure that research pertinent to women's health is identified and addressed through research activities supported by NIH. The ORWH works with the NIH Institutes, Centers, and Divisions by supporting research on health issues of concern to women.

The Office of Minority Programs develops NIH-wide goals for minority research and training, directs and coordinates these programs and, through the NIH Institutes, Centers and Divisions, supplements awards that increase minority participation in research and support pilot projects that identify effective methods to disseminate information to improve minority health.

The Office of Science Policy and Legislation (OSPL) provides leadership and guidance to NIH programs concerning science policy, program planning, program evaluation, health economics and the development and implementation of health legislation. The Office also provides staff direction and support to the Advisory Committee to the Director, NIH, and coordinates math and science education initiatives for NIH.

The Office of AIDS Research, which coordinates both the NIH intramural and extramural AIDS research effort, is a centralized locus for various AIDS-related policy and operating functions and represents the Director, NIH, on AIDS-related matters.

There are also a number of administrative and managerial support functions in the Office of the Director:

The Office of Communications plans and directs activities designed to achieve better understanding of NIH programs and accomplishments on the part of the general public, Congress, biomedical institutions and the medical profession. This office also coordinates the public affairs and other communication activities of the Institute, Centers and Divisions.

The Office of Equal Opportunity is responsible for providing policy direction, planning and monitoring of the Equal Opportunity Program. The office develops the NIH Affirmative Action Program and monitors its implementation in cooperation with NIH components and is also responsible for the administrative processing of complaints of discrimination, including the resolution of informal disputes.

The Office of Administration is the component of the OD responsible for providing leadership and guidance in all phases of management. This office provides central services to the NIH in the areas of budget and financial management, personnel management, management policy, grant and contract administration, management evaluation and review, procurement and logistical support.

Overall Budget Policy

The FY 1993 budget request for the Office of the Director is $203,430,000. This represents an increase of $61,318,000 above the FY 1992 appropriation of $142,112,000. This request includes $45,000,000 to establish the Minority Health Initiative to expand on NIH's continuing efforts to improve the overall health of minorities by focusing on infant mortality, health behaviors of adolescent and young adult minorities, aging and minority biomedical training programs. The request also includes $10,236,000 for the Office of Minority Programs, which serves as the focal point for coordinating the overall NIH policies and programs for improving minority health status and expanding the participation of minorities in biomedical or health service delivery careers. The request also includes $44,494,000 for the Women's Health Study, which will study the leading causes of death and disability among women;--cancer, heart disease, and osteoporosis--in post-menopausal women, and $10,240,000 for the Office of Research on Women's Health, which has been charged with designing and setting an NIH research agenda on women's health and assuring that women are appropriately represented in clinical research. Other highlights include $20,000,000 for the Director's

Discretionary Fund, $14,256,000 for the Academic Research Enhancement Award (AREA) Program, $2,126,000 for the Diagnostic Radiology Research Program, $14,372,000 for the AIDS Research Program, $40,726,000 for the central OD program offices and $1,980,000 for Science Education.

The request includes 685 FTEs, an increase of twenty over the FY 1992 level of 665. The increase in FTE's will support the Minority Health Initiative (2 FTEs), the Women's Health Study (4 FTEs), the Office of Human Subjects Research (4 FTEs), the Office of Science Integrity (5 FTEs), the Science Education Program (2 FTEs), the Office of Research on Women's Health (1 FTE) and the Minority Programs (2 FTEs).

Trans-NIH and Program Support Activities

The pursuit of scientific excellence often extends across organizational lines and many research and research related administrative activities involve two or more Institutes, Centers or Divisions. The Office of the Director coordinates these trans-NIH activities, provides leadership for NIH-wide initiatives, and in addition, provides program support services to all NIH components. Examples of these efforts in which the OD plays the central role include the following:

Women's Health Study

The Women's Health Study (WHS) has been established in the OD to study the leading causes of death and disability among America's women. This is a major trans-NIH initiative that addresses the prevention of cancer, heart disease, and osteoporosis in post-menopausal women. Studies will be implemented in three segments that will include: a large clinical trial measuring low fat dietary patterns, hormonal replacement therapy and calcium/vitamin D supplementation; a longitudinal observational study of 70,000 to 100,000 women to assess predictors and biomarkers of these diseases; and a community trial to test approaches to adoption of healthful behaviors. These studies will provide scientifically validated information for women and providers of their health care, on preventive approaches-both personal and medical-on conditions that represent the major cause of death, disability, and impaired quality of life. Conceptual development and initial planning for the WHS has been completed and plans are in the review stage. The plans were developed by 40 scientific staff representing 10 institutes at NIH and were coordinated by the Office of the Director, NIH, through the Office of Disease Prevention and Office of Research on Women's Health. The planning has been reviewed by the Director, NIH, an Executive Committee of Institute Directors, and in a public hearing held on October 28 and 29, 1991. Review comments have been evaluated by the planning group, and where possible, have been incorporated in a revised conceptual plan. Plans are now available for both the clinical trial, the observational study and the community trial segment.

Community studies targeted to improving health behaviors have previously been conducted in the United States with interventions related to decreasing cardiovascular risk (supported by the National Heart, Lung, and Blood Institute). These cardiovascular studies indicate that significant beneficial changes can occur with community programs. The community programs planned for the Women's Health Study will benefit from the lessons gained in these studies, but will differ in several important respects. There will be a focus on communities with substantial minority and underserved populations. This segment of society has had little or no beneficial change in risk status in contrast to non-minority and upper income groups. The focus will be on behaviors and conditions of interest to women 45 years of age and older.

The clinical and community trials will be supported through the contract mechanism. A solicitation for proposals will be announced and investigators invited to respond according to specifications in the request. These proposals will be reviewed competitively and the most meritorious selected for funding. The solicitation for the clinical trial and the observational study will be conducted first. It is estimated that one coordinating center and 50 clinical centers will be funded. When these centers have been selected, the final protocol will be developed collaboratively, and common recruitment and training programs will be set up.

The development of this plan and the subsequent management of the study will be coordinated by the Office of Disease Prevention and Office of Research on Women's Health, both of which are under the Office of the Director, NIH. An oversight committee made up of persons having a broad range of relevant expertise and background will review and monitor progress and conduct of all aspects of the studies. This committee will report to the Director, NIH. Separate data and safety monitoring committees will be set up for the clinical trial and observational component and for the community trial.

These committees will meet about every 6 months to monitor the progress of recruitment; status of data management, toxicity, and adverse effects; and evidence of efficacy. They will recommend to the Director, NIH, whether to continue or stop the studies.

Minority Health Initiative

The Minority Health Initiative (MHI) is being established in FY 1993 to build upon NIH's previous efforts to improve the overall health of minorities. The MHI will focus on infant mortality, health behaviors of adolescent and young adult minorities, aging, and minority biomedical training programs.

A total of $5,000,000 is included in the MHI for the infant morbidity and mortality component. Despite gains in neonatal medicine and overall improvement in infant mortality rates, black infants continue to be twice as likely to die within the first year of life as white infants. This can be clearly seen in the District of Columbia, which has the nation's highest infant mortality rate. The MHI will support the intramural Perinatal Research Branch, National Institute of Child Health and Human Development (NICHD), located off-campus in D.C. Research in this Branch will bring the best of perinatal science to bear on premature labor, toxemia, and other problems that are more frequent among minorities and contribute to the disparate infant mortality rates.

The MHI will include $5,000,000 to fund community-based intervention studies. While many think of adolescence as a time of good health and low mortality rates, the picture for minorities is very troubling. Not only are death rates higher for minority youth, but homicide is the leading cause of death. Rates of death by homicide are almost ten times higher for black than white youth. Homicide and other forms of violence take their toll among other minorities, and among women as well as men. NIH is creating an initiative that will focus on health behavior interventions aimed at conflict resolution skills. Other health behavior, including that related to obesity, sexually transmitted diseases (STDs), and adolescent pregnancy, would also be included in these community-based interventions.

A total of $5,000,000 will address the array of health problems where young adult minorities suffer disproportionately. It is clear that early health and screening and improved compliance with therapies--drug or behavioral--are needed. Hypertension, renal disease, obesity, periodontal disease, STDs, glaucoma, and other problems that are much more prevalent among minorities can all be detected by health screening and treated effectively if medical and behavior regimens are observed. Research to develop more effective methods to get minority young adults into health screening and comply with prescribed medical and behavioral treatments will be the focus of research in the minority health initiative directed toward young adults. While the OMP, working closely with NICHD, is leading these initiatives, both the adolescent and young adult phases will involve most of the Institutes.

The $5,000,000 MHI program segment on aging will be a multi-faceted research and research training program aimed at improving the health status of older minority persons and at increasing the numbers of minority investigators with careers on research in aging. The objective of the targeted research is to increase the knowledge of aging processes in minority populations and thereby reduce morbidity and disability among older minorities. Although more minority elderly are living into the older ages, for many of these individuals there is extensive morbidity and frailty.

The remaining $25,000,000 for the MHI will focus on minority biomedical training programs and will include: the Pre-college Program; the Community and Junior College Program; the Minorities in Majority Schools Program; the MS - PhD Training Program; and the Extramural Associates Graduates Awards.

Research on Women's Health

Actions to produce recommendations to better address research on women's health have been initiated by NIH through the Office of Research on Women's Health (ORWH). The ORWH is under the supervision of the Director, Office for Research on Women's Health, a position that was filled in FY 1991. The staff completed several critical activities in support of its mandate to design and set an NIH research agenda on women's health and to assure that women are appropriately represented in clinical research. To achieve its mandate on a trans-NIH research agenda and in preparation for the workshop, the Office held a public hearing in which 60 organizations interested in women's health testified on a women's health research agenda at NIH. An additional 30 organizations responded in writing. The recommendations from the public hearing were incorporated into the design of the ORWH workshop, Opportunities for Research on Women's Health. This workshop convened over 120 scientists, clinical researchers, ethicists, economists, and clinicians who considered gaps in research on women's health and made recommendations for such an agenda at the NIH for the next several decades. The proceedings are being prepared and will be available early in FY 1992.

The ORWH provides funds to other NIH Institutes, Centers, and Divisions for augmenting new research initiatives or expanding current studies to address high priority areas regarding women's health and increase accrual of women in studies. The ORWH received 41 nominations for supplemental funding from the ICDs and awarded 20 supplemental grants in 1991.

The ORWH has taken a number of steps to strengthen and implement the NIH policy on the inclusion of women in biomedical and biobehavioral studies. The NIH Guide to Grants and Contracts, revised and implemented in February 1990, is being monitored closely in the first year of operation and is being revised as necessary based upon the responses from Initial Review Groups, NIH Scientific Review Administrators, and NIH Advisory Councils. The revised guidelines, which are being developed in cooperation with the Office of Minority Programs and the Office of Extramural Research, are presently under review and should be available in early FY 1992.

The ORWH is preparing to address two critical issues in women's health research through workshops in 1992: 1) the Recruitment, Retention, and Promotion of Women in Science, and 2) Institutional Review Boards (IRBs) and NIH Policy on the Inclusion of Women in Biomedical Research. This committee is developing a program to achieve greater participation of women in science. The ORWH is cooperating with the Institute of Medicine to consider a workshop on the medical, legal, and ethical issues of using women, particularly those of childbearing age, in biomedical research.

Minority Programs

The mandate of the Office of Minority Programs (OMP) in the Office of the Director, NIH, is to serve as the focal point for coordinating overall NIH policies and programs for improving minority health status and expanding the participation of minorities in biomedical or health service delivery careers. The Associate Director for Minority Programs (ADMP), in collaboration with all ICDs, produced a comprehensive assessment of NIH efforts relative to minority health, including existing programs and activities, and indicated opportunities for improvement. Using this assessment, OMP developed a four-year plan indicating priorities for increased support for minority health and training programs. This plan is being incorporated into the overall Five-Year Strategic Plan of the Director of NIH. As a follow-up on the comprehensive report, and as part of the groundwork for the four-year plan, 53 distinguished scientists, scholars, and educators were appointed to a fact-finding team and were charged with presenting to the Director, NIH, the interests, concerns, and priorities of the minority communities at large. OMP also organized and conducted three regional meetings attended by a broad-based constituency of nearly 1,000 persons who provided their counsel as well. At the conclusion of these regional meetings, the team drafted recommendations for immediate and long-term action and submitted them to the ADMP.

Human Subjects Research

The Office of Human Subjects Research (OHSR) is being established within the Office of Intramural Research to coordinate and oversee the entire NIH human subjects protections system in order to ensure that research involving human subjects is carried out uniformly at NIH in accordance with the Code of Federal Regulations Title 45 Part 46 Protection of Human Subjects. In FY 1991 the position of Director for OHSR was created and an Acting Director was appointed to serve throughout the recruitment process to select a permanent Director. Other efforts include the drafting of a "Comprehensive Plan of Action to Create a Unified System of Human Subjects Protection at the NIH" which is undergoing review by an advisory committee of clinicians, scientists and administrators. The plan will be presented for approval to the Director, NIH, the ICD Directors and the Scientific Directors. A Clinical Research Advisory Committee has been formed to review selected protocols involving human subjects for consistency of quality control.

Science Education

Through OSPL and its Office of Science Education Policy, the OD will continue its leadership role with the NIH Institutes, Centers, and Divisions (ICDs), the Federal Coordinating Council for Science, Engineering, and Technology Committee on Education and Human Resources, and the PHS Life Sciences Education and Science Literacy Board to refine and develop science education and public science literacy DHHS initiatives. In addition, the new programs pilot tested in FY 1991 -- Science Education Partnership Award (SEPA), Biomedical Research Advancement: Saturday Scholars (BRASS), and Science Alliance -- will be evaluated. Decisions will be made for modifying, expanding, and packaging these programs for wider dissemination.

OSPL is also working with the National Cancer Institute to expand their successful Summer Science Enrichment program, to make this into a nationwide activity. A Request For Proposal will be announced to implement this pilot effort.

Unconventional Medical Practices

NIH initiated activities to review the current status of unconventional medical practices. Each of the Institutes, Centers, and Divisions have appointed an individual to serve as a contact on this issue. This working group will meet for the first time in January 1992 to review current programs and offer recommendations to implement the legislative mandate.

An Ad hoc Subcommittee on Unconventional Medical Practices of the Advisory Committee to the Director, NIH will be formed to develop a response to the concerns addressed by the Senate. The ICDs have been asked to identify specific research efforts receiving support from NIH that are related to the assessment or validation of unconventional medical practices. Each of these research efforts will be reviewed by the Subcommittee to determine the appropriate studies needed to evaluate the unconventional medical practices.

One area of particular interest is an assessment of the therapeutic effectiveness of acupuncture. The American Academy of Medical Acupuncture, with endorsement from the American Medical Association, has invited NIH to participate in a scientific workshop to design a controlled clinical research program to assess the medical uses of acupuncture. This activity could lead to an authoritative statement on proven indications of acupuncture treatment.

Another joint venture with the National Science Foundation, the Agency for International Development, the National Cancer Institute, and the Fogarty International Center at NIH involves broadening developing countrys' involvement in the sustainable use of natural products for biomedical applications. This activity is linked to biodiversity conservation and tropical ecosystem preservation.

NIH Office of Education

NIH established the NIH Office of Education (OE) within the Office of Intramural Research to develop and coordinate intramural education and recruitment programs in the biomedical sciences for participants ranging from the most advanced postdoctoral levels down to precollege levels. Established in June of 1990, the OE quickly evaluated current programs and developed new initiatives to address recruitment and training problems. In the recruitment and training arena, the OE directed efforts to accredit six residency programs in the subspecialties of internal medicine; developed and implemented a coordinated media campaign to raise visibility of NIH opportunities which included publishing and distributing the first comprehensive NIH Postdoctoral Research Opportunities catalog; and developed and implemented the NIH-International Medical Scholars Program which enables foreign medical graduates to receive training in clinical and basic research at the NIH. These efforts resulted in more than doubling the number of applications received centrally for clinical programs and increased significantly the number of positions filled.

It is well recognized that investments in the educational pipeline for postdoctoral fellows must begin very early. For that reason the OE established and coordinated a variety of science programs for students and teachers. These include the NIH Biomedical Research Preparatory School which offers training for students from high schools with significant minority enrollments. This Saturday program runs for two months, trains students in sophisticated techniques of molecular biology, and prepares them for research internships. Another program enables students and teachers to participate in research projects for a full year. New programs for pre-service and in-service teachers are planned for the summer of 1992 and will provide training in molecular biology, teaching techniques, and a research experience. The OE also established the NIH Science Education Academy composed of teachers, scientists, and OE staff to develop courses, instructional materials, and videos for use on campus and across the country. The OE has also created NIH EdNET, an electronic bulletin board for science education. In a variety of electronic conferences, students and teachers can receive teaching materials, science reviews, lists of teaching resources and assistance from the NIH community. All of these systems utilize the strengths of the NIH research community to reach out to students and teachers across the country as well as locally to attract students into biomedical research.

Academic Research Enhancement Award Program

The NIH makes special efforts through the Academic Research Enhancement Award (AREA) Program to stimulate research in educational institutions that provide the baccalaureate training for a significant number of our nation's research scientists, who historically have not been major recipients of NIH support. The AREA Program is designed specifically to enhance the research environment at those institutions by supporting new research projects or expanding ongoing research activities in areas related to the health sciences. In FY 1991 141 AREA awards amounting to $13.7 million were issued, as compared to 118 awards totaling $11.4 million for the previous year.

Other Trans-NIH and Program Support Activities

Several demonstrations under the Federal Demonstration Project will be completed and evaluated in FY 1992. The Federal Demonstration Project is aimed at improving the effectiveness of noncompeting funding determination and the requirement for universities to maintain equipment inventories. In conjunction with the overall assessment, the NIH will evaluate the noncompeting continuation process to identify what information is needed in today's research environment to determine scientific progress and financial accountability and what is the most efficient way to collect this data. The NIH will also evaluate the current financial reporting system and propose suggestions to the PHS/HHS for improving the quality and timeliness of financial reports.

Through the Office of Recombinant DNA Activities (ORDA), OSPL will continue its principal role in relation to review of Federal policy on the conduct of recombinant DNA research, facilitating compliance with a uniform set of guidelines for such research. The Recombinant DNA Advisory Committee (RAC) and the Human Gene Therapy Subcommittee (HGTS) have begun studying ways to streamline the review process because of the rapid increase in the number of human gene therapy protocols. The HGTS has recently voted to merge itself with the RAC in order to create a single step review process at the national level. The RAC will vote on the merger in February, 1992. If agreed to by the RAC, a one year transition period is anticipated to complete the merger. During this time, the HGTS will continue its study of policy issues.

The Office of Communications has completed two pilot videotapes for a proposed series of 13 short vignettes, called "Profiles of Biomedical Science," for viewing on cable and commercial television. The primary goal of the series is to encourage young people to consider careers in biomedical research. Each "profile" will feature a working biomedical scientist or student scientist speaking about his or her own ideas and discoveries. These pilot vignettes will be used to explore marketing possibilities for the series. An important byproduct of this communications effort will be to improve public understanding of biomedical research. The series will convey a variety of pertinent messages: science can be an exciting, fulfilling career; good science requires highly trained people, the right environment and financial backing; and the process of medical science sometimes moves slowly and unpredictably. The series will also serve, when appropriate, as a vehicle for conveying correct perceptions about the welfare and use of animals in research.

The Office of Disease Prevention (ODP) provides leadership, direction, and support to science and biomedical programs that seek to improve the nation's health through research, research training, and the international exchange of knowledge. Five consensus development conferences and two technology assessment conferences were conducted in FY 1991. Through these conferences, the safety and effectiveness of emerging and established technologies are assessed and discussed in a public forum. Topics of recent conferences include Treatment of Panic Disorders; Recognition and Treatment of Depression in Late Life; Gastrointestinal Surgery for Severe Obesity; and Dental Biomaterials. To augment popular press coverage of consensus panel recommendations, the office began to use a news placement service, which reaches over 3,000 local and suburban daily and weekly newspapers. With respect to nutrition research, the office served as co-lead with FDA in the implementation phase of the nutrition objectives of Healthy People 2000: National Health Promotion and Disease Prevention Objectives. The office also sponsored seven disease prevention seminars for the NIH community, including Teenage Tobacco Use and Oral Health; Risk Taking and Adolescent Sexual Behavior; Patterns and Consequences; Challenges in Stroke Prevention Research; and SIDS: Working Toward Preventive Strategies. Finally with the Fogarty

International Center, the ODP initiated and coordinated disease prevention information for transmission to Eastern Europe and the Soviet Union through the Voice of America.

To more fully implement provisions of the Federal Technology Transfer Act, the Office of Technology Transfer (OTT) has developed and implemented a number of programs during FY 1991 to further technology transfer. The OTT has negotiated the first license agreement for a patent developed under a CRADA related to genetic therapy. Genetic therapy techniques will revolutionize the way medicine is practiced and the way drugs are delivered. NIH intramural patent applications and other CRADAs on new genetic therapy techniques have resulted in the successful completion of the first licensing agreement. OTT's newest model license agreement has accelerated the process of licensing unpatented biological materials. NIH's Office of General Counsel has determined that NIH may license these materials to commercial entities under the Public Health Service Act. The OTT directory of contacts of potential licenses has been expanded to include more than 2,000 entries.

AIDS Research Program

The purpose of the Office of AIDS Research (OAR) is to coordinate NIH intramural and extramural AIDS research; centralize various AIDS-related policy and operating functions; and represent the Director, NIH, on AIDS-related matters. An additional major function of the office is the development and coordination of the NIH budget request for AIDS. Other efforts include: developing information strategies with interagency collaboration to inform the public of NIH AIDS research activities, and recommending solutions to ethical/legal issues; fostering national and international information exchange with government, industry, and academia concerning AIDS research; and management of the NIH Loan Repayment Program for AIDS researchers. Activities performed by the OAR include the following:

- The OAR conducted the seventh and eighth meetings of the AIDS Program Advisory Committee (APAC), which advises the Secretary, Assistant Secretary of Health, the NIH Director, the NIH AIDS Coordinator, and the NIH AIDS Executive Committee on short- and long-term planning needs for AIDS research.

- The OAR coordinated the development of a draft NIH Strategic Plan for HIV-Related Research and presented the Plan to the APAC for review and consideration.

- At the direction of the NIH Director, a centralized, administrative research information system for AIDS was designed and implemented. This agency-wide system to track and categorize the funding of AIDS research is named the AIDS Research Information System (ARIS). Data for FY 1989 through FY 1991 have been collected and reposited in the ARIS. An online inquiry system has been developed and has been demonstrated to its targeted users in the Office of the Director. The response has been most favorable.

- The NIH AIDS Research Loan Repayment Program (LRP), mandated by P.L. 100-607, was implemented in FY 1990, in part, to counter the economic disincentives to embark on research careers. The LRP provides repayment of accumulated educational debt, up to a maximum of $20,000 per year, as well as a 39% tax reimbursement of the amount of loans repaid, to individuals recruited as employees to the NIH to engage in AIDS-related research. During FY 1991, 15 researchers/physicians entered into initial two-year service contracts and four entered into one-year renewal service contracts, bringing the total number of LRP participants to 34. The NIH-wide program totals 34 participants, including researchers/physicians from the following ICDs: NIAID, NCI, NINDS, NICHD, NIDR, NEI, NHLBI, and the CC. It is anticipated that an additional 20 participants will be selected each in FY 1992 and FY 1993.

NIH Intramural AIDS Targeted Antiviral Program

The NIH Intramural AIDS Targeted Antiviral Program (IATAP) was established in the Office of the Director to support basic research on the structure and function of the human immunodeficiency virus (HIV). The goal of the program has been to utilize the methods of structural biology, molecular biology, and biochemistry to develop new agents that can be used in the treatment of and vaccine development for AIDS. The general approach is to seek information from these basic studies that will facilitate design of new drugs that interfere with the virus life cycle by blocking the function of the HIV proteins or nucleic acids. The understanding of how HIV proteins and nucleic acids function should also contribute to improved therapies through the development of new methods for drug screening and by the identification of new molecular targets for antiviral agents.

Many of the very best scientists at the NIH have been attracted by the IATAP to work on AIDS for the first time. At present 49 separate research groups from 12 different Institutes are being supported by the program. Structural biology projects include the determination of the three-dimensional structure of HIV proteins in both crystal and solution by state-of-the-art X-ray crystallography and nuclear magnetic resonance methods. Biochemical studies include elucidation of the molecular mechanism of the viral enzymes--reverse transcriptase, ribonuclease H, and protease. All three enzymes are unique to the virus and are therefore excellent targets for drugs. Molecular biology studies are concerned with the mechanism of integration of the viral DNA into the host DNA, the mechanism of activation of the provirus and the control of expression of the viral DNA, and the cellular processing and modification of the viral polypeptides to form the functioning viral components. Progress reports on all current studies were presented at the annual two-day NIH Intramural AIDS Targeted Antiviral Workshop held in October, 1991.

Highly purified proteins are required for many of the structural, physico-chemical and pharmacological studies being conducted by participants in the program. To meet this need the Protein Expression Laboratory (PEL) is now established in Building 6B, staffed with two senior scientists, three technicians and a secretary. Work on RNase H, reverse transcriptase, REV, TAT, protease and integrase is proceeding in collaboration with several different groups in five Institutes, and seven other proteins are also being studied.

Major research accomplishments during the past year by investigators supported by the program include:

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- Determination by nuclear magnetic resonance of the complete three-dimensional structure in solution of the two zinc finger domains of the p7 nucleocapsid protein of HIV. This protein packages the RNA in the virion, and disruption of its function is a potential therapeutic strategy.

- Development of a simple assay for the activity of the HIV integrase. Several pharmaceutical companies are now setting up the assay to screen for potential therapeutic inhibitors of this enzyme.

- Discovery that the high error rate in reverse transcription is due to mechanisms in addition to the absence of a proofreading function. This work provides a deeper understanding of the extreme diversity of HIV.

- Further development of the fusion protein of soluble CD4 with a powerful bacterial toxin selectively to kill cells expressing HIV, and demonstration in vitro that it has a synergistic effect in combination with AZT. Site-directed mutagenesis of the fusion protein has improved both its cytotoxic activity and survival.

Office of the Director

Research Management and Support

Authorization Legislation - Title IV, Section 402(b) of the Public Health Service Act. 1992 Authorization: Indefinite

FY 1991 Actual		FY 1992 Appropriation		FY 1993 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
638	$97,650,000	658	$142,112,000	678	$203,430,000	+20	+$61,318,000

The Office of the Director supports research and research training in the biomedical sciences through the formulation and coordination of NIH policy. Funding for the Office of the Director during the last five years has been as follows:

	Amount
FY 1988	$61,819,000
FY 1989	72,201,000
FY 1990	89,916,000
FY 1991	97,650,000
FY 1992	142,112,000

Rationale for the Budget Request

The FY 1993 budget request for the Office of the Director is $203,430,000 an increase of $61,318,000 over the FY 1992 Estimate of $142,112,000. Following are recent accomplishments, current activities and future plans for the following programs:

Policy and Direction Offices

The FY 1993 request for the Office of Research on Women's Health (ORWH) will enable this office, with a budget of $10,240,000 and a staff consisting of a Director and a staff of 7 employees, to implement its charge: to establish a trans-NIH research agenda for women's health in close cooperation with the Institutes, Centers, and Divisions, and to monitor the appropriate inclusion of women in NIH-supported research. The majority of the $10,240,000 will be directed toward this research agenda on women's health research. Remaining dollars will be directed primarily toward: the ORWH and IOM study on medical, legal, and ethical issue surrounding the inclusion of women in clinical studies; a public hearing and workshop on the recruitment, retention, re-entry, and advancement of women in biomedical careers; a planning meeting to consider recruitment, retention, and follow-up of women, particularyly minority women, in clinical studies; further interaction with Institutional Review Board organizations to consider the implications of including women, especially those of childbearing age, in clinical studies; and other meetings and initiatives, as necessary, to implement, enhance, and promote the NIH research agenda on women's health, the inclusion of women in research studies, and the role of women in biomedical/biobehavioral endeavors.

The Office of Minority Programs (OMP), under the direction of the Associate Director for Minority Programs, is the focal point for coordinating overall NIH policies and programs for improving minority health status and expanding the participation of minorities in biomedical or health service delivery careers. The request will enable the OMP to operate with a staff of eight employees with a budget of $10,236,000. In FY 1993 OMP will be focusing on two primary initiatives which are the Minority Life Span Health Initiative and the Minority Human Resource Development Initiative. The first initiative focuses on the major health problems across the life span of minority Americans which include infant mortality, health behaviors of adolescent and young adult minorities, and problems of older minorities. The second initiative focuses on the development, recruitment, and retention of minorities in the broad range of careers in biomedical research and health services delivery.

The increase of $106,000 for ethics initiatives will support efforts with the Office of the General Counsel to conduct effective and specialized ethics training at the agency; to develop and issue guidance on all ethics matters; to oversee the administration of the public and confidential financial disclosure systems; to counsel employees on all ethics matters; to coordinate all ethics activities within the NIH; and to act as a liaison between the NIH and the Special Counsel for Ethics and the Office of Government Ethics.

Women and Minority Health Studies

The FY 1993 request provides $44,494,000, an increase of $19,747,000, for the Women's Health Initiative (WHI). This is a trans-NIH initiative that addresses the prevention of cancer, heart disease, and osteoporosis in postmenopausal women. There are three components: a large clinical trial testing preventive interventions in women; an observational study of 70,000 to 100,000 women to define new predictors of these diseases; and a community study to evaluate how to promote healthful behaviors. The clinical trial will evaluate a low fat dietary pattern to prevent breast and colon cancer; hormonal replacement therapy to prevent heart disease and osteoporosis; and calcium/vitamin D supplementation to prevent osteoporosis and colon cancer. The community study will investigate strategies to improve lifestyles that prevent disease and to increase screening and identification of early disease. The outcome of these studies will be scientifically validated advice to women and their health care providers regarding prevention of the most common causes of death and disability and proven strategies to implement adoption of healthful behaviors. The studies will be supported by contracts awarded competitively to about 60 study centers throughout the United States. The first 15 to 20 contracts will be awarded to vanguard centers in FY 1992 and the next 40 to 45 contracts will be awarded in FY 1993. The three components of the study will be initiated by the vanguard centers and the studies will be fully operational with the addition of centers in FY 1993.

The request also provides $45,000,000 to establish the Minority Health Initiative (MHI). The increase provides $5,000,000 for research on infant mortality with research efforts directed towards premature labor, toxemia, and other problems that are more frequent among minorities. The increase also provides $5,000,000 for a focus on health behaviors of adolescent minorities by looking at health behavior interventions aimed at conflict resolution skills. With regards to young adult minorities, the MHI is providing $5,000,000 for research to develop more effective methods to get minority young adults into health screening and comply with prescribed medical and behavioral treatments. The MHI is also providing $5,000,000 for a multi-faceted research and research training program aimed at improving the health status of older minority persons and in training increased numbers of minority investigators for careers in research on aging. The remaining MHI focus will be minority biomedical training programs and will include $25,000,000 for the following: the Pre-college Program; the Community and Junior College Program; the Minorities in Majority Schools Program; the MS - PhD Training Program; and the Extramural Associates Graduates Awards.

Science Education

The request includes $1,980,000 for the Science Education Program to increase the level of science literacy in the United States and to influence the supply of scientists and technicians to meet future national needs. In FY 1993 $1,000,000 will be used for the Science Education Partnership Awards (SEPA) which is a program that encourages the development of creative partnerships between educators and researchers. The remaining funds will be used to support programs to further PHS science education goals and those identified through the FCCSET Committee on Science Education and Human Resources. For example, NIH will contribute its share to support PHS-wide and FCCSET initiatives; and pilot and evaluate initiatives such as the Biomedical Research Advancement: Saturday Scholars (BRASS) program, a Saturday morning science education program for middle school students; and the Science Alliance, a special adopt-a-school program which partners Elementary school science teachers with PHS scientists to enhance the teaching of the life sciences at the Elementary school level. NIH will expand its partnership efforts and continue to expand linkages with other Federal agencies and with a wide variety of non Federal entities. For example, a cooperative program with the Indian Health Service to allow their scholarship recepients to take their extern assignment in an NIH laboratory; and the development of programs with local school systems and academic institutions for training teachers who will work with researchers to help integrate new biomedical science teaching materials into the classroom, who can speak creditably about specific classroom situations and who can take leadership roles in training with colleagues and working with local school districts.

Other Biomedical Research and Health Sciences Issues

Numerous issues in biomedical research and the health sciences will continue to require the attention of the offices and divisions within the OD. These include the following initiatives:

The Office of Scientific Integrity (OSI) was established in FY 1989 to serve as a focal point within PHS for overseeing the implementation of policies and procedures designed to safeguard the integrity of research conducted and supported by PHS agencies. In FY 1993 the functions performed by OSI will continue to receive priority attention and support by the PHS. Substantive and procedure improvements will continue to be made in PHS scientific initiative functions. The increase of $255,000 will support the functions of the office and an additional 5 FTEs.

The Office of Human Subjects Research (OHSR) has been established to coordinate and oversee the entire NIH human subjects protection system in order to ensure that research involving human subjects is carried out uniformly at NIH in accordance with the Code of Federal Regulations Title 45 Part 46 Protection of Human Subjects. An Acting Director is currently coordinating the OHSR and it is anticipated that a Director will be appointed during FY 1992. The increase of $395,000 in FY 1993 will support an additional 4 FTEs and a strong emphasis will be placed on expanding the educational training program of intramural scientists in the conduct of human subjects in FY 1993.

AIDS Research

In FY 1993 the Office of AIDS Research (OAR) received an increase of $671,000 over the FY 1992 level. The increase provides for mandatory costs and will allow the OAR to continue current program initiatives.

The OAR will continue to serve as the focal point for AIDS research within the Office of the Director. The Office plays a key role in developing and operating the management process needed for coordination of the NIH AIDS research program.

The OAR plans to expand the AIDS Research Information System (ARIS) to link to other NIH databases including international activities and to the National Library of Medicine's AIDSLINE database. The information staff of the ARIS will continue to reach out to the ICDs to offer assistance with their mainframe information systems.

The OD AIDS funds will continue to support the IATAP at approximately the same level as FY 1992. In order to promote continuity in the program, projects are generally approved on a two-year basis. Forty-six of the 49 projects funded in FY 1991 will continue to be supported in FY 1992. Two projects have terminated because the principal investigators have left NIH, and two new projects have been approved in FY 1992, for one year only. All projects currently supported will have to compete for renewed two-year funding in FY 1993. It is expected that 80-85% of these projects are likely to merit continued support at approximately the same dollar level. It is also expected that at least another 45 proposals will be submitted for review. Between one-quarter and one-third of these new proposals will probably be highly rated by the review panel and recommended for funding.

It is vital for the program to obtain the three-dimensional structures for the important proteins encoded by the HIV virus so that a rational plan for the development of agents which inhibit these proteins can be constructed. The PEL will increase production of the highly purified HIV proteins needed by the program's projects and provide additional capabilities in structure determination. To expand the X-ray crystallographic studies, the development of two new X-ray crystallography laboratories, one in NIAMS and one in NIAID, is being supported by the IATAP. The structures will eventually be submitted to medicinal chemists and pharmacologists for the development of drugs that may inhibit the important enzymes necessary for HIV's infectivity and reproduction.

Diagnostic Radiology

The request includes $2,126,000 for the Intramural Diagnostic Radiology Research Program, established in 1990 to serve as the focal point and training program promoting basic research in the medical imaging for the intramural radiology community. The Diagnostic Radiology Research Program provides individuals with formal training medical imaging (i.e., radiologist, nuclear medicine, image processing) the opportunity to develop research skills and techniques which will ultimately result in highly motivated scientists returning to in the academic radiological community. The program operates a "state of the art" Magnetic Resonance Imaging unit devoted exclusively to research in operational and scientific investigations utilizing magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) to study functional and metabolic changes in normal and disease processes. The 1.5 Tesla whole-body MR unit will also facilitate the development of new techniques, methods, and capabilities for in vivo MRI and MRS. Research training of functional and metabolic studies examining the brain, heart, kidney and other organs by MRI/MRS are also correlated to metabolic and tissue perfusion studies of Positron Emission Tomography (PET) and other diagnostic imaging techniques in nuclear medicine.

A state of the art computer image processing system is under development with the capabilities of manipulating and combining all diagnostic imaging modalities into a single display of the relevant anatomy, physiology and metabolic function of the normal and disease tissue. State of the art laboratory facilities which will include a radiopharmaceutical and biological area, chemistry and tissue culture facility for tissue and cell receptor analysis are being considered. Currently, an Acting Director is coordinating the Diagnostic Radiology Research Program while an active recruitment effort for a permanent Director is underway.

Transfer Authority

In FY 1993 a change in the OD appropriation language, pertinent to the NIH Director's 1 percent transfer authority, is being requested to provide transfer authority for high priority activities as the Director may so designate, in lieu of transfer authority for emergency activities. This change will allow the Director more flexibility to apply funds to meet significant research opportunities and high priority initiatives.

DHHS - NATIONAL INSTITUTES OF HEALTH
Detail of Permanent Positions
Office of the Director

	1991 Actual	1992 Estimate	1993 Estimate
Executive level IV	1	1	1
ES-6	3	3	3
ES-5	4	5	5
ES-4	10	13	13
ES-3	2	2	2
ES-2	0	0	0
ES-1	0	0	0
Subtotal	19	23	23
GS/GM-15	45	46	48
GS/GM-14	66	67	71
GS/GM-13	103	105	113
GS-12	83	85	86
GS-11	33	34	35
GS-10	7	7	7
GS-9	38	39	39
GS-8	25	26	26
GS-7	82	84	86
GS-6	41	42	42
GS-5	37	38	39
GS-4	22	23	24
GS-3	4	4	4
GS-2	1	1	1
GS-1	0	0	0
Subtotal	587	601	621
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	0	0	0
Director Grade	12	12	12
Senior Grade	4	4	4
Full Grade	0	0	0
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	16	16	16
Ungraded	0	0	0
Total permanent positions	623	641	661
Unfilled positions, end-of-year	0	0	0
Total permanent employment, end-of-year	623	641	661

NATIONAL INSTITUTES OF HEALTH

Office of the Director

New Positions Requested

	FY 1993		
	Grade	Number	Annual Salary
Research Management and Support			
Assistant to Associate Director	GS-15	1	66,610
Director, Office of Human Subjects Research	GS-15	1	66,610
Health Science Administrator	GS-14	1	56,627
Program Analyst	GS-14	2	113,254
Contract Specialist	GS-14	1	56,627
Program Analyst	GS-13	2	95,840
Contract Specialist	GS-13	4	191,680
Operations Specialist	GS-13	1	47,920
Investigator	GS-13	1	47,920
Program Analyst	GS-12	1	40,299
Paralegal	GS-11	1	33,623
Secretary	GS- 7	2	46,948
Files Manager	GS- 5	1	18,340
Clerk Typist	GS- 4	1	18,579
		20	900,877

AMOUNTS BUDGETED FOR INCREASES IN FULL - TIME EQUIVALENTS

ACTIVITY / POSITIONS	GRADE	NO. OF POS	O.C. 11 ANNUAL SALARY	O.C. 12 BENEFITS @ 15.0%	O.C. 21 TRAVEL	O.C. 23.1 23.2 RENT	O.C. 25 OTHER SERVICE	O.C. 31 EQUIPT	OTHER OBJECTS	SUB TOT NEW COSTS	SUPPORT STAFF SHARE	NO. OF FTE	TOTAL NEW COSTS
OD Program Support													
Ass't. to Associate Director	GS-15	1	66,610	9,992	2,500		2,000	6,000		87,102		1	87,102
Office Chief	GS-15	1	66,610	9,992	2,500		2,000	6,000		87,102		1	87,102
Case Worker	GS-14	1	56,627	8,494	1,300		2,000	6,000		74,421		1	74,421
Program Analyst	GS-14	2	113,254	16,988	2,000		4,000	12,000		148,242		2	148,242
Contract Specialist	GS-14	1	56,627	8,494	1,000		2,000	6,000		74,121		1	74,121
Program Analyst	GS-13	2	95,840	14,376	2,000		4,000	12,000		128,216		2	128,216
Contract Specialist	GS-13	4	191,680	28,753	4,000		8,000	24,000		256,433		4	256,433
Operations Specialist	GS-13	1	47,920	7,189	1,000		2,000	6,000		64,109		1	64,109
Investigator	GS-13	1	47,920	7,189	1,000		2,000	6,000		64,109		1	64,109
Program Analyst	GS-12	1	40,299	6,045	1,000		2,000	6,000		55,344		1	55,344
Paralegal	GS-11	1	33,623	5,044	1,000		2,000	6,000		47,667		1	47,667
Secretary	GS-07	2	46,948	7,042	300		4,000	12,000		70,290		2	70,290
Files Manager	GS-05	1	18,340	2,751	200		2,000	6,000		29,291		1	29,291
Clerk-Typist	GS-04	1	18,579	2,787	200		2,000	6,000		29,566		1	29,566
		20	900,877	135,136	20,000	0	40,000	120,000	0	1,216,013	0	20	1,216,013

The request includes 685 FTEs, an increase of twenty over the FY 1992 level of 665. The increase in FTE's will support the Minority Health Initiative (2 FTEs), the Women's Health Study (4 FTEs), the Office of Human Subjects Research (4 FTEs), the Office of Science Integrity (5 FTEs), the Science Education Program (2 FTEs), the Office of Research on Women's Health (1 FTE) and the Minority Programs (2 FTEs).

NATIONAL INSTITUTES OF HEALTH

Office of the Director

Advisory and Assistance Services

For FY 1993, the Advisory and Assistance Services budget will be $3,024,000 an increase of $662,000 over FY 1992. These funds will continue to support the NIH Program Evaluation Fund and the Acquired Immunodeficiency Syndrome Program Advisory Committee.

The Office of the Director, NIH, is responsible for the NIH program evaluation funds which are authorized by Section 513 of the Public Health Service Act. Program evaluation funds are to be used at the discretion of the Secretary, HHS, for the evaluation of health programs. These evaluation studies aim to assist in program development and management decision making. The budgeted amount includes the NIH Program Evaluation funds which are totally reimbursed from the NIH ICDs. The estimate does not include the funds for the Office of the Assistant Secretary for Health or the Office of the Secretary.

The Office of the Director supports the Acquired Immunodeficiency Syndrome Program Advisory Committee. Consultant services requirements are necessary for the compensation of non-federal committee members. This committee is authorized by law and chartered by the Secretary, HHS. The advisory committee provides knowledgeable advice, suggestions, and criticisms of ongoing and proposed NIH AIDS research activities to the Secretary, HHS, the Assistant Secretary for Health and the Director, NIH.

All requisitions charged against the NIH Program Evaluation Fund must be reviewed and approved by the Planning and Policy Research Branch. All consultant services obligations are reviewed and reconciled against the approved consultant services ceiling and the quarterly report issued by the Operations Accounting Branch, DFM.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

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NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

For construction of, and acquisition of equipment for, facilities of or used by the National Institutes of Health, including the acquisition of real property, [$103,840,000] *$72,518,000*, to remain available until expended.

(Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 1992.)

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NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

Amounts Available for Obligation [1/]

	1991 Actual	1992 Appropriation	1993 Estimate
Appropriation.............	$172,853,000	$103,840,000	$72,518,000
Section 514(b) reduction..	-4,166,000	---	---
Sequester order...........	-2,000	---	---
Subtotal, adjusted appropriation.........	168,685,000	103,840,000	72,518,000
Unobligated balance, start of year...........	57,436,000	176,805,000	---
Unobligated balance, end of year.............	-176,805,000	---	---
Total obligations....	49,316,000	280,645,000	72,518,000

1/ Excludes the following amount for reimbursable activities carried out under this account: FY 1991 -- $6,847,000.

Buildings and Facilities

Summary of Changes

1992 Estimated budget authority	$103,840,000
1993 Estimated budget authority	72,518,000
Net change	-31,322,000

Increases:

A. Program:

1. Infrastructure Modernization & Improvement Program	+$9,225,000
2. Clinical Center Modernization	+3,750,000
Total increases	+12,975,000

Decreases:

A. Program:

1. Rehabilitation of Laboratory Buildings 2, 3, 4, 5, 7, and 8	-$15,560,000
2. Intramural Animal Facilities	-6,000,000
3. Waste Handling Facility, NIEHS	-2,000,000
4. NIEHS Additions to Facilities	-10,050,000
5. AIDS Facilities	-7,000,000
6. Repairs and Improvements	-3,687,000
Total decreases	-44,297,000

Total, Net Change	-31,322,000

NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

Budget Authority by Activity
(Dollars in thousands)

	1991 Actual	1992 Appropriation	1993 Estimate
Research facilities.................	$40,431	$136,665	$19,300
Service and administrative facilities........................	8,885	143,980	53,218
Total obligations.................	49,316	280,645	72,518
Unobligated balance, start of year..	-57,436	-176,805	---
Unobligated balance, end of year....	176,805	---	---
Total budget authority.............	168,685	103,840	72,518
HIV/AIDS...........................	(9,502)	(7,000)	(---)

NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

Budget Authority by Object

	1992 Appropriation	1993 Estimate	Increase or Decrease
Printing and reproduction............	$50,000	$---	-$50,000
(Obligations)........................	(50,000)	---	(-50,000)
Other services.......................	103,790,000	72,518,000	-31,272,000
(Obligations)........................	(280,595,000)	(72,518,000)	(-208,077,000)
Total budget authority by object.....	103,840,000	72,518,000	-31,322,000
(Total obligations by object)........	(280,645,000)	(72,518,000)	(-208,127,000)

NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1992 Amount Authorized	1992 Appropriation	1993 Amount Authorized	1993 Budget Request
Funded Authorizations:						
Buildings and Facilities............	Title IV, Section 402(b)	40§282	Indefinite	$103,840,000	Indefinite	$72,518,000
Total Budget Authority..				103,840,000		72,518,000

NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

Appropriation History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1984	$19,900,000	$24,980,000	$25,100,000	$25,040,000
1985	11,100,000	21,730,000	21,700,000	21,730,000
1986	14,900,000	14,900,000	14,900,000	14,900,000
1986 Sequester				-641,000
1987	8,000,000	31,900,000	31,900,000	31,900,000
1988	5,000,000	30,000,000	50,000,000	47,870,000
1989	5,000,000	20,000,000	12,500,000	38,532,000
1990	21,600,000	81,600,000	41,600,000	61,600,000
1990 Sequester				-558,000
1991	86,903,000	239,903,000	68,803,000	168,687,000 2/
1991 Sequester				-2,000
1992	104,125,000	108,625,000	89,485,000	103,840,000
1993	72,518,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.

2/ Excludes enacted administrative reduction of $4,166,000.

Justification

Buildings and Facilities

	1991 Actual	1992 Appropriation	1993 Estimate	Increase or Decrease
Research facilities.......	$84,533,000	$54,160,000	$19,300,000	-$34,860,000
Service and administrative facilities..............	84,152,000	49,680,000	53,218,000	+3,538,000
TOTAL................	168,685,000	103,840,000	72,518,000	-31,322,000

General Statement

This appropriation provides for the design, construction, improvements and major repair of clinical, laboratory, and office buildings and supporting facilities essential to the mission of the National Institutes of Health. Funds are provided for non-recurring direct construction projects as well as ongoing major repairs and improvements. All funds are available until expended.

Construction of facilities for the National Institutes of Health spans a period of nearly 56 years, dating back to legislation that authorized Building 1 in June 1936. Facilities funded under this appropriation include those required for both research programs and support services at the main NIH Reservation in Bethesda, Maryland, totaling 77 buildings and more than seven million gross square feet of space. Additional facilities are the Frederick Cancer Research and Development Center, Frederick, Maryland; the NIEHS facility in Research Triangle Park, North Carolina; the Gerontology Research Center, Baltimore, Maryland; the NIH Animal Center located in Poolesville, Maryland; the Rocky Mountain Laboratory, Hamilton, Montana; Primate Facilities at Perrine, Florida, New Iberia, Louisiana, and Sabana Seca, Puerto Rico.

The NIH is coping with an aging, deficient physical plant. The majority of our infrastructure systems are between 20 to 40 years old and are undersized and beyond their design life. While we have taken action to minimize the risk of imminent collapse, failure of one or more central systems would mean closing down significant elements of our research program for extended periods of time. To address these deficiencies and plan for the future, the NIH is integrating all corrective and new construction programs into a comprehensive Facilities Revitalization Program. The intent of this program is to develop a long-term strategy to coordinate programs and set priorities so that ongoing laboratory and clinical research as well as anticipated growth can be supported in accordance with modern standards. If the NIH intramural research program is to remain at the forefront of biomedical and health research, our facilities and supporting utilities must be modernized and improved in order to provide an adequate infrastructure to support the research mission of the agency.

Initial construction of the South Campus facilities at the National Institute of Environmental Health Sciences (NIEHS) in North Carolina began in 1976. During construction, a number of contractual disputes arose between the Government and Turner Construction Company and its subcontractors. These disputes eventually developed into full litigation before the Armed Services Board of Contract Appeals (ASBCA).

Although these disputes occurred from events between 1976 through 1981, the consolidated case was not heard before the ASBCA until the summer of 1985. In January 1990, the ASBCA ruled in favor of the prime contractor and subcontractors on all issues of liability. DHHS appealed the Board's ruling to the United States Court of Appeals for the Federal Circuit; but the decision by the Board was upheld.

This court decision found that NIH owed the contractor and subcontractors a total of $25,000,000. Since the Court found in favor of the claimants, they were paid the $25 million from the Claims for Contract Disputes account of the Department of the Treasury. The Departments of HHS and Treasury have worked out an arrangement whereby HHS will forward $4 to $5 million per year, starting in FY 1993, to the Claims for Contract Disputes account of the Department of the Treasury until the debt is satisfied.

Within the total request of $72.5 million, $4 million will be reallocated from the requested Buildings and Facilities projects to accommodate this required payment. Details on the requested modifications of this request will be made available shortly to the Committee once they have been identified on pages 238-242.

In the future, NIH will monitor construction awards by establishing controls to minimize the recurrence of this kind of action.

Following are the Buildings and Facilities appropriation levels for the last 5 years:

	Amount
FY 1988	$47,870,000
FY 1989	38,532,000
FY 1990	61,042,000
FY 1991	168,685,000
FY 1992	103,840,000

Purpose and Method of Operation

The Buildings and Facilities appropriation funds two major requirements of the NIH biomedical research endeavor: the design and construction of new facilities for NIH research programs and the continuing repair and improvement of existing facilities. Long-term projects currently under construction include campus infrastructure modernization and improvement, modernization/safety improvements of the NIH Clinical Center, rehabilitation of the campus' oldest laboratory buildings, renovation of existing animal facilities, the Child Health and Neurosciences Facilities Program, and AIDS related construction. Design of the William H. Natcher Building was awarded in November 1991, and construction award for Phase I is anticipated in September 1992.

Overall Budget Policy

The 1993 budget request of $72,518,000 reflects the high priority placed on biomedical research and intramural facilities revitalization by the Secretary, Department of Health and Human Services. The program includes funding for the infrastructure modernization and improvement program, continuation of safety improvements and correction of urgent central utility system deficiencies under the Clinical Center modernization program, rehabilitation of a group of 50 year-old laboratory buildings, and the upgrading of animal facilities to meet the standards of the American Association for Accreditation of Laboratory Animal Care (AAALAC). The request also provides for the routine repair and improvement of facilities.

Buildings and Facilities

Research Facilities

Authorizing Legislation - Section 402 of the Public Health Service Act.
1993 Authorization: Indefinite.

Budget Authority:

1991 Actual	1992 Appropriation	1993 Estimate	Increase or Decrease
$84,533,000	$54,160,000	$19,300,000	-$34,860,000

This activity provides for the design and construction of facilities for the NIH research programs. Ongoing construction projects within this activity include the continuing renovation of the Clinical Center; renovation of six of the campus' older laboratory buildings; consolidation, renovation, and construction of existing animal facilities; Child Health and Neurosciences Facilities; and AIDS related construction. Initial construction will begin in 1992 for replacement of the aging facilities leased by the National Institute of Environmental Health Sciences.

Following are the Research Facilities appropriation levels for the last 5 years:

	Amount
FY 1988	$36,935,000
FY 1989	18,772,000
FY 1990	54,885,000
FY 1991	84,533,000
FY 1992	54,160,000

Rationale for the Budget Request

The FY 1993 budget request for Research Facilities is $19,300,000, a decrease of $34,860,000 from the FY 1992 appropriation of $54,160,000. The basic thrust of the 1993 budget request is to improve safety, to reduce obsolescence to allow state-of-the-art research, to ensure patient care is in compliance with the Joint Commission on Accreditation of Health Care Organizations (JCAHO) standards, and to ensure the care and use of animals is in compliance with American Association for Accreditation of Laboratory Animal Care (AAALAC) standards.

Clinical Center Modernization

FY 1993 Budget Request... $7,400,000

The orientation of the Clinical Center modernization project was reevaluated and has been modified to focus on safety concerns, central building utilities, and JCAHO accreditation. The 1993 request will fund the completion of the areas of refuge (to maintain accreditation) and the renovation of two ventilation systems to be covered under the essential short-term ventilation upgrade program. In addition, the 1993 request will fund the design for the secondary distribution of the newly enhanced chilled water main.

Projects currently funded are a sprinkler system for the Clinical Center, replacement of the aging fire alarm system, and increased capacity of the diagnostic radiology ventilation system. The replacement of the G-Wing exhaust system is scheduled for completion in March 1992.

Rehabilitation of Laboratory Buildings

FY 1993 Budget Request... $1,400,000

In FY 1993, funds are requested to provide for the design of Building 3 as part of the long-range goal of the Buildings and Facilities Program that provides for the major renovation of six laboratory buildings that have been operational for approximately 50 years. This modernization is required to assure a safe operating environment for state-of-the-art research; to provide structures that meet new life safety codes; to accommodate needs of the handicapped; and to improve levels of air purity, temperature stability, energy conservation, and other requirements in support of modern biomedical research.

The exterior of the buildings are structurally sound, but the building infrastructure systems and interior architectural features and layouts are obsolete. The strategy used to accomplish this renovation is to renovate one building while designing the next building. As each building is completed, the programs from the next building to be renovated are moved to the newly renovated space.

By 1996, the rehabilitation of 4 of the 6 laboratory buildings will be complete. Buildings included in this project and their completion dates are: Building 8, March 1986; Building 4, August 1988; Building 5, scheduled for completion August 1992; and Building 2, scheduled for completion in 1996, with Buildings 3 and 7 remaining. Potential out-year costs for this project total $37.02 million in current (escalated) dollars.

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Intramural Animal Facilities

FY 1993 Budget Request.. $10,500,000

The NIH is currently involved in a significant program to ensure that all animal facilities on the NIH campus meet AAALAC standards. This has grown from the increased public concern over the use of animals in research and NIH's concern that its own facilities meet AAALAC guidelines for the housing and use of animals in research. Funds in 1993 will provide for the addition to Building 103 and the construction of an Indoor/Outdoor Primate Habitat at the NIH Animal Center (NIHAC) at Poolesville, Maryland.

The initial phase of the NIH plan for upgrading intramural animal facilities has been completed. It involved constructing new buildings, 6B on the NIH campus and 110A at the NIHAC; major renovations in Buildings 10A and 36; and smaller renovations in Buildings 7, 14D, 29A, 30, and 41. The cost of this phase was $24.5 million.

Design is underway for the renovations of Buildings 28 and T-8 (NIHAC). Renovations to Buildings 14B, 14C, 14E, and NIHAC Building 100 as well as additions to Buildings 102 and 103 (cagewash facility) are in the planning stages with design expected to start in FY 1992. In addition, design is expected to start in late FY 1992 on the small ungulate facility and the sewage treatment plant expansion, both located at the NIHAC.

The NIH AAALAC site visit occurred in November 1991. The opinion of NIH management is that AAALAC will grant NIH provisional accreditation for a 2-year period. The AAALAC stipulated that the NIH must continue its program of facility rehabilitation in order that the provisional accreditation status be granted. The second and final phase to secure provisional accreditation will total $48.3 million.

Buildings and Facilities

Service and Administrative Facilities

Authorizing Legislation - Section 402 of the Public Health Service Act.
1993 Authorization: Indefinite.

Budget Authority:

1991 Actual	1992 Appropriation	1993 Estimate	Increase or Decrease
$84,152,000	$49,680,000	$53,218,000	+$3,538,000

This activity includes the continuing program of repairs and improvements to existing buildings and facilities that house research and administrative activities. This activity also provides for the design and construction of new facilities for the NIH service and administrative programs including funds for the planning, design, and the first phase of construction of the William H. Natcher Building.

Following are the Service and Administrative Facilities appropriation levels for the last 5 years:

	Amount
FY 1988	$10,935,000
FY 1989	19,760,000
FY 1990	6,157,000
FY 1991	84,152,000
FY 1992	49,680,000

Rationale for the Budget Request

The FY 1993 budget request for Service and Administrative Facilities is $53,218,000, an increase of $3,538,000 over FY 1992. This activity provides for the program of repairs and improvements to existing facilities and implementation of the infrastructure modernization and improvement program for the site utilities at the Bethesda campus that is critical to the continued usage of the NIH research facilities.

Infrastructure Modernization and Improvement Program

FY 1993 Budget Request.. $42,600,000

This request is the third year of a nine-year effort to upgrade the central plant and distribution systems. The FY 1993 request will continue the upgrade of the existing plant and begin to expand/replace the chilled water and steam distribution systems. Remaining funding necessary to complete the program is estimated at $114.4 million in current (escalated) dollars.

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The Infrastructure Modernization and Improvement Program (IMIP) is a key element of the NIH Facilities Revitalization Program. The IMIP was developed to carryout the replacement and expansion of the central plant and utility distribution systems. Its goals are to correct safety deficiencies, restore and improve reliability, expand capability, and improve the efficiency of the utility systems.

Major infrastructure deficiencies include refrigeration equipment age and capacity limitations, boiler equipment age and capacity, undersized and/or deteriorated steam and chilled water distribution piping systems, widespread presence of asbestos as an insulation material, and excessive operating costs. An independent review of the IMIP conducted by the U.S. Army Corps of Engineers concluded: "The Review Committee is convinced, following the review of available documents and on-site investigations, that the infrastructure at the NIH Bethesda campus is in need of major repair and/or replacement." Work must expeditiously continue to correct these repairs, if curtailment of service or unscheduled outages are to be avoided.

Less critical but significant problems exist in other central utility systems. Recent studies of the electrical and sanitary systems indicate that deficiencies exist in these systems. An evaluation of the scope of deficiencies, repair/replacement strategies, and appropriate funding sources is underway. Studies of the potable water, storm water, and other central systems will be initiated with the development of the NIH Master Plan.

Repairs and Improvements

FY 1993 Budget Request.. $10,618,000

The Repairs and Improvements (R&I) program provides for major repairs and improvements to the physical plants of all Federally owned NIH facilities. The costs for some of the projects are recurring and substantial. For example, some projects such as roofs, roads, structures, and building and underground utilities require repairs to preserve or achieve sound conditions. For other projects, the costs are largely one-time expenditures for major items of equipment requiring unpredictable (emergency) repair or replacement such as transformers, chillers, and cooling towers. In addition, this program supports adjustments to the infrastructure utility systems to provide necessary capacity to accommodate changes in the direction of mandated research. Typically, these repairs or replacements require immediate attention, and thus are not suited to a schedule of expenditures such as found in the Infrastructure Modernization and Improvement Program (IMIP).

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ISBN 0-16-038559-8

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